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EDITORIAL.

It is with profound sorrow that we announce the sudden death of Dr. Max A. Goldstein, founder and managing editor of THE LARYNGOSCOPE, at his summer home at Frankfort, Mich., July 27, 1941.

Under his efficient editorship and management THE LARYNGOSCOPE has become a journal of international importance, representative of the highest standards in its special field. Its publication will be continued according to Dr. Goldstein's wishes and under the same ethical policies as inaugurated by him at the time of its inception.

His far-sightedness in appointing its splendid editorial staff a few years ago insures its permanency as one of the world's leading journals in oto-rhino-laryngology. Very shortly an editor will be appointed, who, in collaboration with this staff, will assume the editorial duties of the office. Under the direction of this group THE LARYNGOSCOPE will continue to present to the literature of its special field the same fine quality of original papers and ethical advertising as has been its custom for nearly fifty years and become a fitting monument to its founder, Dr. Max A. Goldstein.

VITAMINS AND THE EYE, EAR, NOSE AND THROAT.

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In this informal talk* we will discuss this subject in general, and then offer a definite approach to therapy, in our specialties.

In a vague and general sense, it has been realized for years that the human being throughout the world has not been ingesting the right foodstuffs. Something has been wrong. Aside from the tragedy of starvation or semi-starvation in so many parts of the earth today, even those individuals who are able to buy whatever foods they wish are nevertheless receiving improperly balanced diets — through innocence or inattention. Among such people there has been no difficulty as to the calories — provided by the proteins, carbohydrates and fats; and on the average, it appears that the content of minerals has also been more or less adequate. Only in the past few years has it become increasingly evident that the fundamental lack has been in the vitamins — those definite chemical food substances which, although they are present in the body in almost negligible amounts, are nevertheless necessary for life itself.

World War No. 1 went a long way towards wrecking civilization; however, because of immediate and pressing necessity, it was the very making of the science and art of Aviation. The press of events during the four years of that European war advanced Aviation by scores of years. Now, in World War No. 2, by the same urgent necessity, there is a speeding up of the study and the use of vitamins; so that it seems probable that our knowledge of the vitamins will be similarly advanced by scores of years. In all the countries at war, and in our own effort of National Defense, vitamins are not only playing a prominent rôle, but are now recognized as essential for the well-being not only of the military forces but of civilians as well. It is not too much to hope that such advances in the next few years may result in an appreciable benefit to the human race — (or what is left of it).

*Presented before the Mid-Winter Clinical Course of Ophthalmology and Otolaryngology of the Research Study Club of Los Angeles, Jan. 23, 1941; and before the Pacific Coast Oto-Ophthalmological Society, May 26, 1941.

Old Gaul was "divided into three parts." It would seem that all modern medical literature might actually be divided into two: — that on the vitamins and that on all the other subjects! The mass of work on vitamins is almost unbelievable, and the number of pathologic conditions for which vitamins are prescribed — by soda fountains, department stores and beauty shops — is almost equally unbelievable. Such prescribing might be termed "Bridge Club Therapy." In the United States alone, of the 100 million dollars a year spent for bottles of vitamins, we should pause to consider what percentage of it is justifiable. One per cent? Surely not over five.

In a previous article,[1] an attempt was made to deduce some facts on which we can rely in our routine practice. We already are sure that no vitamin improves any condition that has not been caused by a lack of the same vitamin. In brief, "No deficiency — No cure." For example, if any lesion of the eye, ear, nose or throat is entirely due to syphilis, tuberculosis, neoplasm, a neuroma of the VIII Nerve, focal infection, or drugs such as quinine — it is certainly an idle and expensive gesture to prescribe vitamins.

On the contrary, however, we also know that the proper ingestion of vitamins will prevent many pathologic states in the eye, ear, nose and throat, as elsewhere in the body; and furthermore, that if a lesion is actually due to a lack of a vitamin, that vitamin will cure it. Of course it is a simple matter to demonstrate a vitamin deficiency in certain gross conditions, such as beriberi, pellagra, scurvy and rickets. Such advanced states, however, are so rare that probably none of us will ever see many of them. The difficulty lies in the large number of our patients who have only a moderate or mild deficiency. The entire problem would become utterly simple — and be completely solved — if only we had easy and accurate methods of discovering a moderate or mild deficiency for each of the vitamins.

We derive comfort from realizing that a vitamin is not a drug; so we do not need to be unduly anxious if we prescribe a larger amount of vitamins than the patient needs — with the exception of "D," and in certain instances of some of the factors of the B Complex. If we over-prescribe any of the

other vitamins, the only damage done is to the patient's pocketbook.

Many conditions increase the need for vitamins: If a patient is taking iron or thyroid, the vitamin requirements are increased — because iron and thyroid actually oxidize the vitamins. Similarly, exercise increases the demand. Alcohol supplies a large number of calories but contains no vitamins; therefore, anyone who takes an appreciable amount of alcohol requires an extra amount of vitamins; and the chronic alcoholic may exhibit a desperate need for a large intake.

Nature itself provides the proper foods — adequate in calories, minerals and vitamins. In general, the caloric intake of an individual is adequate, but the vitamin intake is not. It is in the preparing and refining of foods for human consumption that vitamins have been lost — and are still being destroyed. Even in 1941 A.D., we have not yet learned the answers as to the correct preparation of our daily food. The food of our ancestors was far richer in vitamins than ours today; in fact, the phrase so often expressed by our grandfathers might be altered — "Cast thy white bread upon the waters, and hope it will stay there — and *not* return for many days." One of the penalties of our civilization is that we are afflicted with "refined" foods. Ironically, many of these foods which have been artificially deprived of the very vitamins we need, are advertised as "Health Foods." We boil our foods — and extract the vitamins. Of course the water left over after boiling should be used as a basis for soups or for sauces — but in how many homes is this actually done? The modern teaching would be helpful if we really used it: Foods are put in the container; a very small amount of water is added — just enough to provide steam; the lid is put on and the food is then cooked — with no appreciable loss of vitamins or minerals. If vegetables are cooked with the lid off, the vitamins become oxidized; if the lid is left on, the vegetables may lose more of their original color — but they retain more vitamins. Sodium bicarbonate is so frequently used to bring out the original color of green vegetables — and it often intensifies the color; but it destroys the vitamins that require an acid medium, such as "B_1" and "C." Orange juice should not be strained, because the pulp contains more "C" than the juice itself. Moist air in a refrigerator is obviously

better than dry air. In cooling our foods, electric refrigerators extract the moisture from them; if left in long enough, the food becomes actually desiccated. The tender squab finally resembles an Egyptian mummy.

We must bear in mind that no one vitamin affects only one organ or tissue; that patients do not suffer from the lack of only one vitamin; and that in its original form, every article of food contains more than one vitamin. Of course, ideally, we should not prescribe only one vitamin; and we should also prescribe those foods which contain not only the most needed vitamin, but also the other *associated* vitamins.

In our dilemma, is it possible for us to learn the nature of a deficiency by a study of the actual *lesions* that a patient shows? Can we find a rational approach? Perhaps we can — through embryology.

In my own disgust at the vagueness of our therapy — knowing that many of our patients should receive vitamins but not knowing what vitamins to give them — I struggled to find a scientific approach to therapy, and humbly offer it, hoping it will help you in your daily practice as it has helped me. It is the approach through embryology.

The tissues of the ectoderm, mesoderm and entoderm all demand vitamins. Consequently in service to our patients, it is of immediate importance for us to learn all that we possibly can of the observed effects of vitamin deficiency on the derivatives of the three germ layers in the eye, ear, nose and throat.

Although each vitamin does not affect only one structure, yet it appears that each vitamin has a special relation to one germ layer. All three germ layers require vitamins; and the expectant mother should receive a generous supply to be utilized by the ectoderm, the mesoderm and the entoderm of the fetus.

The details of this concept are as follows. Many vitamins seem to have a *preponderant* effect on one germ layer:

"A" ..... on the ectoderm.
"B Complex" ..... on the ectoderm.
"C" ..... on the mesoderm — (connective tissue).
"D" ..... on the mesoderm — (bone formation).

THE DERIVATIVES FROM THE GERM LAYERS.

THE EYE.

Epithelium of lids, cilia, Meibomian glands and lacrimal apparatus	from Ectoderm (surface).
Conjunctiva	from Ectoderm (surface).
Cornea — epithelium	from Ectoderm (surface).
Cornea — stroma	from Mesoderm.
Iris — muscle	from Ectoderm* (surface).
Iris — stroma	from Mesoderm.
Lens	from Ectoderm (surface).
Ciliary muscle	from Mesoderm.
Retina	from Ectoderm (neural).
Choroid	from Mesoderm.
Sclera	from Mesoderm.
Extra-ocular muscles	from Mesoderm.
Aqueous	from Mesoderm.
Vitreous, largely from	Ectoderm.

*All the muscles of the body are derived from the mesoderm, except the iris muscle (and the tiny muscles that "raise the hair"). These are derived from the ectoderm.

THE NOSE.

(1) Epithelium, including the olfactory	from Ectoderm.
(2) Mucous glands	from Ectoderm.
(3) Cavernous structures of turbinates and all supporting tissues	from Mesoderm.

THE MOUTH.

Epithelium	from Ectoderm.
Muscles and bones	from Mesoderm.
Taste-buds	both Ectoderm and Mesoderm.
Tonsils and adenoids	from Mesoderm.
Teeth — enamel	from Ectoderm.
Teeth — dentine and cementum	from Mesoderm.
Salivary glands	from Ectoderm.

PHARYNX AND LARYNX.

Epithelium	from Entoderm.
Supporting tissues	from Mesoderm.

THE EAR.

Internal ear:—

Epithelium, both cochlear and vestibular	from Ectoderm.
Nervous structures	from Ectoderm (neural).
Supporting tissues	from Mesoderm.
Bony otic capsule	from Mesoderm.

Middle ear:—

Epithelium (from first pair of pharyngeal pouches)	from Entoderm.
Ossicles — bone	from Mesoderm.
Ossicles — epithelium	from Entoderm.
Muscles, bone and supporting tissues	from Mesoderm.

Eustachian tube:—

Epithelium	from Entoderm.
Bone and cartilage	from Mesoderm.

If then we note a lesion of the eye, the ear, the nose or the throat, we know of what germ layer this tissue is a derivative — and this gives us an immediate clue as to the vitamin or group of vitamins that are needed. This is the "embryologic approach."

How does this concept seem to fit in with the clinical experience that is available up to this moment? We will first consider the gross pathologic conditions that are well established; and then special conditions in the eye, the ear, the nose and the throat that are also reasonably well established.

BERIBERI, PELLAGRA, SCURVY AND RICKETS:

(1) Thiamin Chloride ..... for beriberi and its polyneuritides — — Ectoderm (neural).
(2) Nicotinic Acid ..... for pellagra — Ectoderm (surface).
(3) "C" — for scurvy — connective tissue of blood-vessels and capillaries, derived from — Mesoderm.
(4) "D" — for rickets — bone, derived from — Mesoderm.

In all of these gross pathologic conditions, the concept seems to be borne out — in that each vitamin appears to have a preponderant effect upon one germ layer.

SPECIAL PATHOLOGIC CONDITIONS OF THE EYE.

"A" — for Xerophthalmia ..... Ectoderm (surface).
"A" — for Nyctalopia ..... Ectoderm (neural).
"B Complex" — especially "B_1" — for retrobulbar neuritis ..... Ectoderm (neural).

Similarly the above vitamins that have been clinically useful in treating these eye conditions appear to fit in with the concept of a preponderant effect of each vitamin on the derivatives of one germ layer.

SPECIAL PATHOLOGIC CONDITIONS OF THE EAR.

External Ear:—
"A" — dry scaly skin ..... Ectoderm (surface).
"B_2" — seborrheic dermatitis ..... Ectoderm (surface).

Internal Ear:—
"B_1" — "B_2" — and nicotinic acid ..... Ectoderm.

Similarly the above vitamins that have been clinically useful in treating these ear conditions appear to fit in with the concept of a preponderant effect of each vitamin on the derivatives of one germ layer.

If this concept is correct, it may become possible for us to reason "in reverse" — although of course such an idea is at present merely theoretical.

"Canker sores" — we reason that these are due to a neuritis (herpes) and we prescribe "B_1," because the nerves are derivatives of the *ectoderm* — (neural).

"Congested turbinates" — "B_1" and "B_2" suggest themselves for a tonic effect on nerve endings; and "C" to lessen intracellular edema by improving the condition of the connective tissue — derived from the *mesoderm*.

"Boggy mucosa of nose and throat" — we think of "B_2" — for its effect on these derivatives of the *ectoderm* and *entoderm*.

"Cracked lips" — we think of "B_2" and nicotinic acid — for their effect on this derivative of the *ectoderm*.

"Pink tooth brush" — if there is no infection we should think of "C" (as in scurvy). Similarly, a tendency to bruise easily suggests "C" — for its effect on the connective tissue of the blood vessels and capillaries — derived from the *mesoderm*.

Some clinical experiments have been made by a few investigators, in producing vitamin deficiencies in the human; but until recently, our precise knowledge has come almost entirely from the laboratory. Such scientific research work on animals constitutes the foundation of our knowledge of the various vitamin deficiencies.

Few of us in clinical practice have had the opportunity to make personal observations of the remarkable effect of depriving animals of vitamins. With such an idea in mind, we conducted experiments with rats.

It also occurred to us that most of the experimental animal work has been for the purpose of discovering each individual vitamin and studying its effects. From the *clinical* stand-

point, however, we realize that no one food contains only one vitamin. Furthermore, a patient may have a particular deficiency in one vitamin, but we already know that he does not lack only this one vitamin, but also other associated vitamins. Therefore, in order to make an approach that would more nearly resemble the clinical condition of patients, yeast was selected instead of just one isolated vitamin. Yeast has another special advantage — it not only contains all the factors of the B Complex which have already been isolated, but it also probably contains other factors of the B Complex which have not yet been isolated. The immediate object of the experiment was to deprive certain rats of the factors of the B Complex and to give the B Complex to the control rats. Instead of the yeast we could have given rice bran, wheat germ, liver concentrate or sugar cane molasses. These also contain the factors of the B Complex; however, yeast provided a convenient method of giving all the factors of the B Complex, known and unknown.

The stock diet is the one used for rats at the University of California at Berkeley. It includes sucrose, vitamin-free casein, Crisco, proper proportions of six mineral salts, and cod liver oil. Rats synthesize their own vitamin C. Consequently this diet provides all the vitamins except the B Complex.

Basic Diet for Rats.

Sucrose — 50 parts.
Casein — 25 parts. } Use ordinary table sugar and vitamin-free casein.
Crisco — 25 parts.

Add: to every 100 gm. of food — salt mixture:

Calcium Phosphate	1.5 gm.
Sodium Chloride	.73 gm.
Potassium Chloride	1.25 gm.
Ferric Citrate	.13 gm.
Sodium Iodide	.03 gm.
Magnesium Sulphate	.7 H_2O — 1.0 gm.

To daily food add 1 per cent cod-liver oil. Give all food and water they want. Make up large supply of basic diet. Make up large supply of salt mixture. Mix daily rations well — food and salt and cod-liver oil.

The main object of the experiment is to make histopathologic studies of the effects of a deficiency in the whole

B Complex. It will be of interest to find out what such a deficiency produces in the ear and to compare these findings with those of Covell,[2] who for six years has made such elaborate studies of the effect of a deficiency in many individual vitamins. The histopathologic findings in the nose, mouth, throat, larynx and trachea are also to be studied — both in the controls and in the deficient animals. This will be of particular interest because to date it appears that no histopathologic studies have been made of the effect of any vitamin deficiency on the structures of the nose or throat.

For the first experiment 12 Wistar stock white rats were secured. They were from two litters, and had the same father. All were strikingly similar in weight and appearance. They had just been weaned, and were 23 days old. Six received the basic diet which provides all the vitamins except the B Complex. The other six rats received the same basic diet *plus* 10 per cent of brewers yeast. Those on yeast doubled their weight in 17 days. The six without the yeast showed no increase in weight after the 17 days — in fact all but one of them weighed less than at the beginning of the experiment. When they appeared to be dying, they then received the yeast for the first time. In two days, they had recovered — not only in weight, but in behavior and general appearance, including a marked improvement in their coats.

This "clinical" observation parallels a recent experience with a patient. A post-graduate student was majoring in education and about to become a teacher; however, he felt he must abandon his life's plan, because he had gradually lost his hearing, equally in both ears, to the extent that he was able to hear only loud conversation. As he now expresses it, "My hearing came back in two weeks, for 89 cents." The therapy was one pound of brewers yeast, for 89 cents, and injections of thiamin chloride. With the improvement in hearing there was an immediate and noticeable relief of "ringing noises" and of a "fluttering sensation" which had disturbed the patient when he was listening to conversation. In this case, the indications for therapy were definite: He was working his way through college and after he had paid for a place to sleep, his tuition, books and carfare, he had little money left for food. For years he had eaten rather little — and what he did eat was obviously deficient in the B Complex. The audiometric curves showed that the hearing

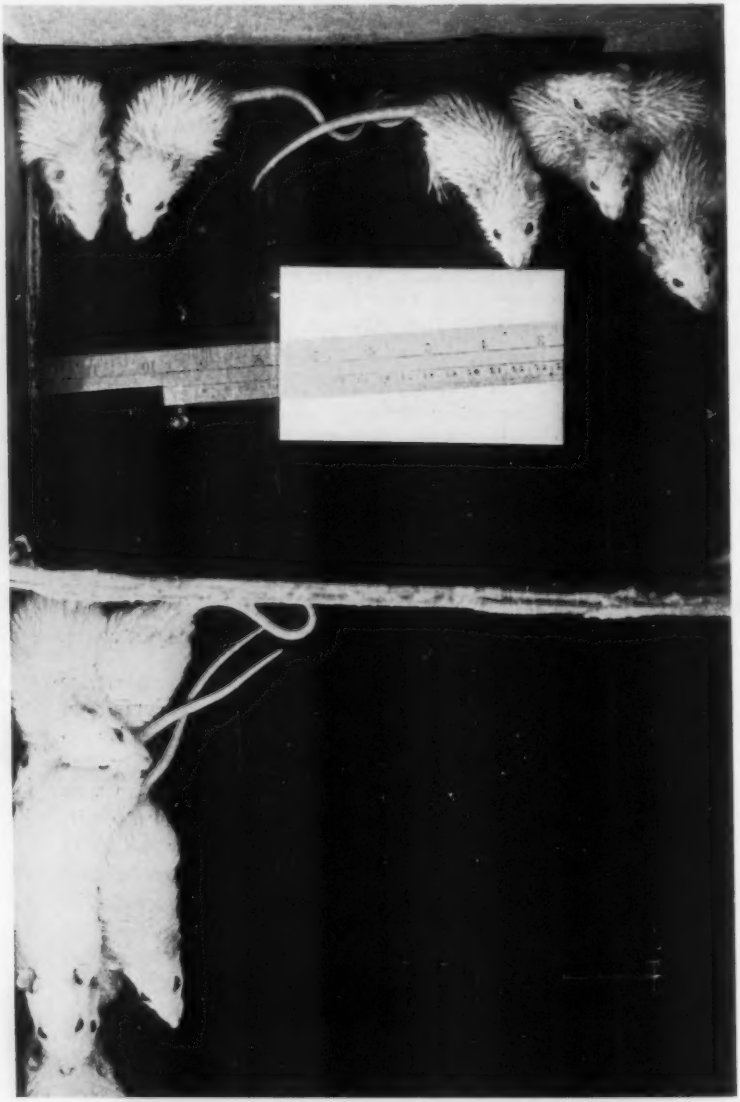

Fig. 1. All the rats were almost identical in weight and appearance at the beginning of the experiment. After 17 days they appeared as above. Those at the left had received yeast; those at the right had received no yeast.

defect in each ear was entirely cochlear. There was a most unusual finding in the audiometric curves. In cochlear lesions caused by constitutional diseases, foci of infection or drugs, we are accustomed to observe a marked impairment in the acuity of hearing for the high tones. Frequently the curve

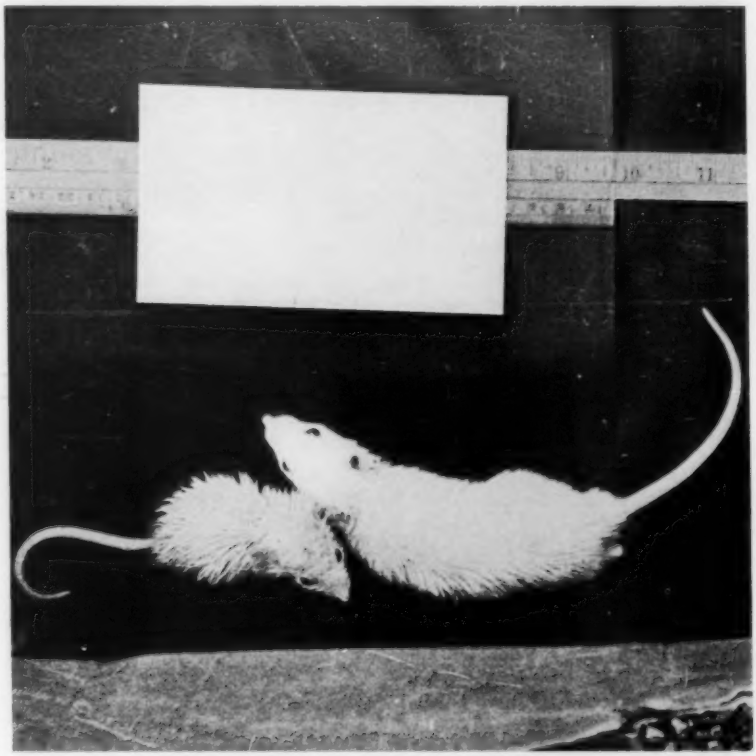

Fig. 2. After 17 days, with and without yeast.

shows a precipitous drop. In this case the curve was "flat" — *i.e.*, there was the same percentage of hearing loss throughout the entire range of hearing. This audiometric curve may possibly prove to be significant if we should find that it is characteristic of a vitamin deficiency. In each ear the entire end-organ was involved. One naturally speculates as to the

location and type of alteration producing the impaired function in such a case. Are the hair-cells affected, the nerve-endings, the ganglia or the VIII Nerve? Is there a localized edema, or a general increase of the fluids within the internal ear? As yet, we do not know. In this case the vestibular tests showed even a greater impairment than the cochlear. There was almost no nystagmus or motion-sensing after turning; and about 5 per cent vestibular function in the right ear and about 10 per cent in the left ear, after the caloric tests. Details of this case, with precision measurements, will be published after a year has passed — and the diagnosis has become established beyond doubt. At the moment, however, we know that there are occasional conditions in which we can improve the hearing by overcoming a deficiency in the B Complex.

After noting the marked improvement in the deficient rats who had received the yeast for only two days, we took away the yeast from five of the larger rats — that had received the yeast from the beginning. In nine days these large rats had reduced in size; and the little deficient rats, continued on the yeast, so increased in size that both sets weighed nearly the same. In this way it proved very easy to "make the big ones into little ones and the little ones into bigger ones," simply by withholding or giving the yeast. It soon became evident that rats cannot even live without the factors contained in yeast.

The purpose of the second experiment consisted in producing moderate and mild deficiencies, over a long period of time. It was first necessary to determine just how much yeast would be required in order to keep the rats alive. To date, it appears that a diet containing 4 per cent of yeast is necessary. It is planned to sacrifice one of the rats from time to time so that specimens of the ear, nose and throat will be available, after different stages of deficiency have been produced. It is important in securing the specimens that the animals be perfused. The technic: First, the animal is anesthetized with sodium amytal; the thorax is rapidly opened; a cannula is inserted into the aorta and tied in place with sutures. A femoral vein is opened. The blood is washed out of the body with normal salt solution until the fluid coming from the open femoral vein is no longer blood-tinged. This part of the perfusion is usually completed in from 5 to

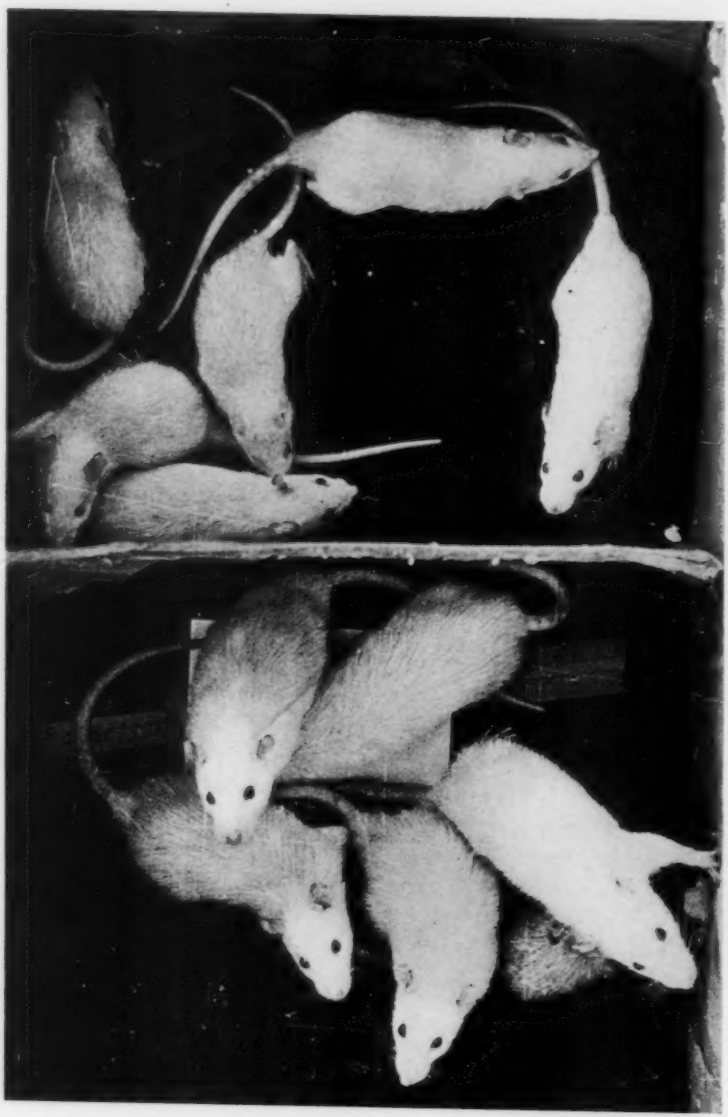

Fig. 3. The deficient rats then received yeast. In 2 days there was a marked improvement in weight and appearance. The restoration to health of the deficient rats is shown in the compartment to the right — after 15 days on yeast.

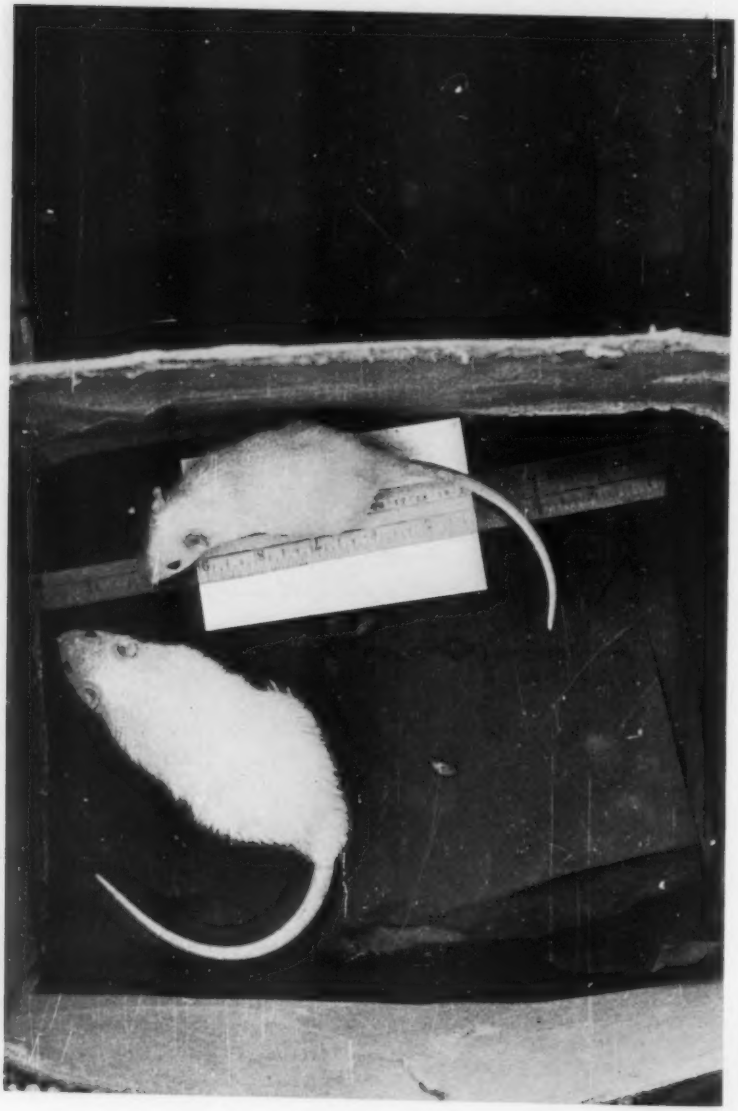

Fig. 4. The deficient rat — to the right of the control rat — has received yeast for 15 days.

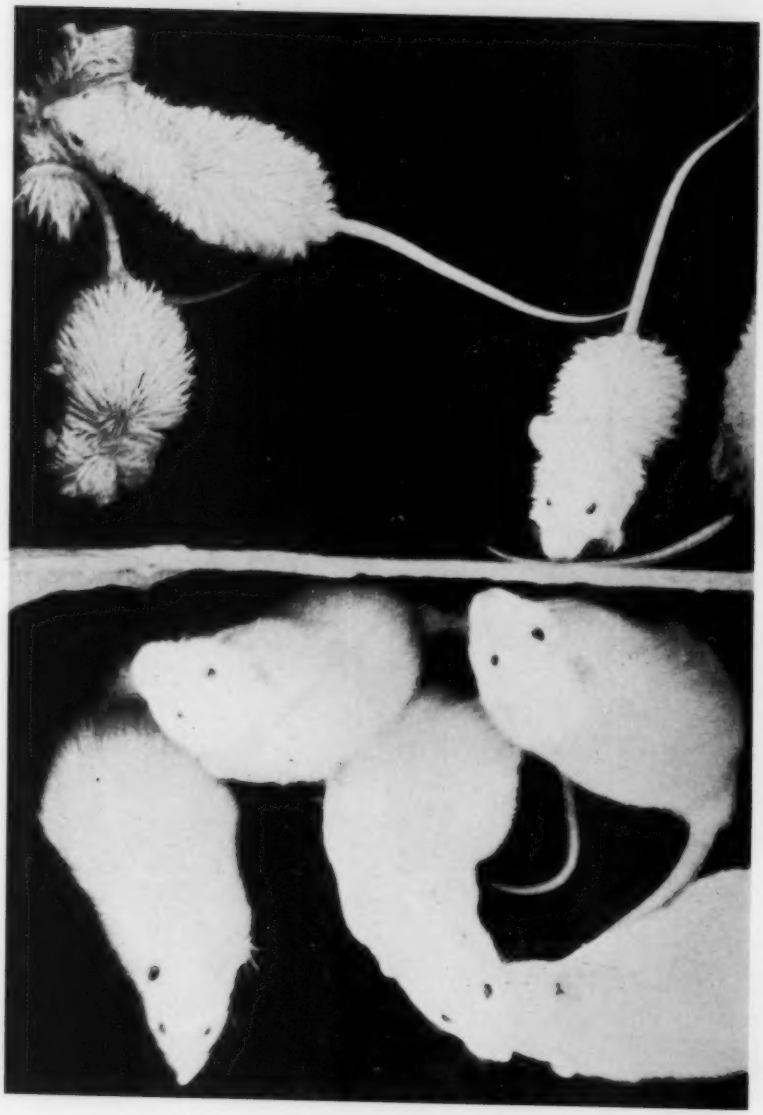

Fig. 5. To the left are the control rats. To the right are the "recovered" rats, who have again been deprived of yeast for 20 days.

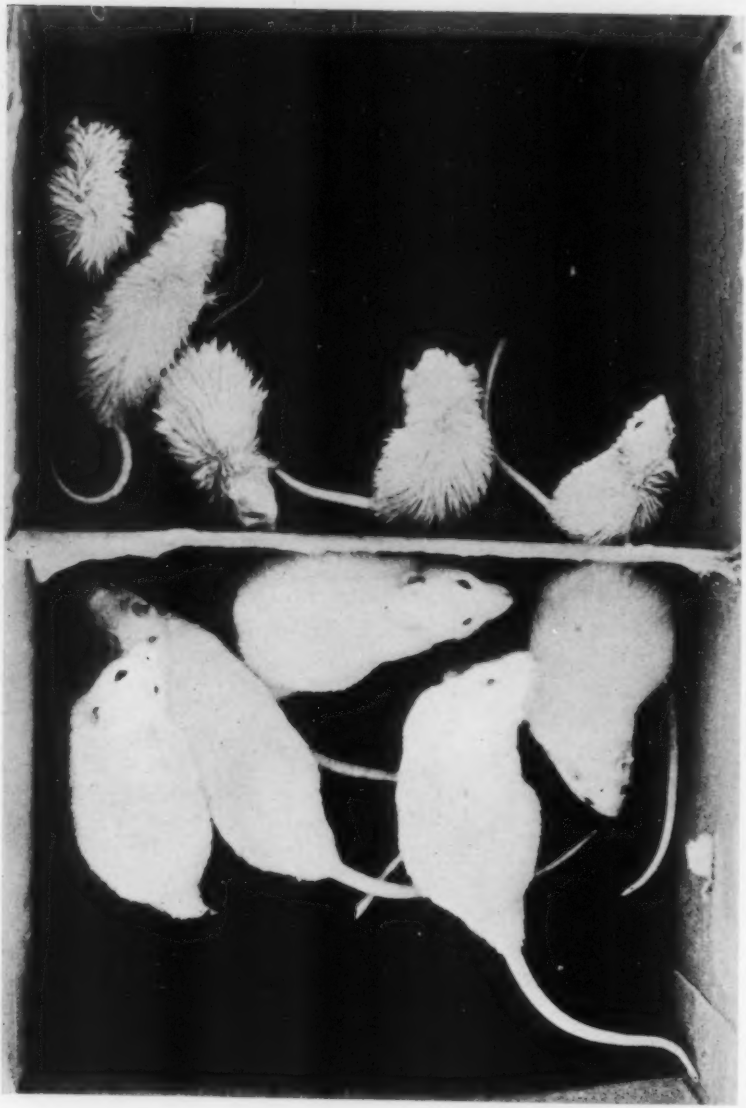

Fig. 6. To the left are five of the control rats that have been deprived of yeast for 9 days. To the right are the "recovered" rats that have been deprived of yeast for 29 days.

10 minutes. A 10 per cent formaldehyde solution is then introduced until fixation is accomplished. This is determined by the onset of rigidity of the entire animal. If the animal is not perfused, histopathologic studies, particularly for the

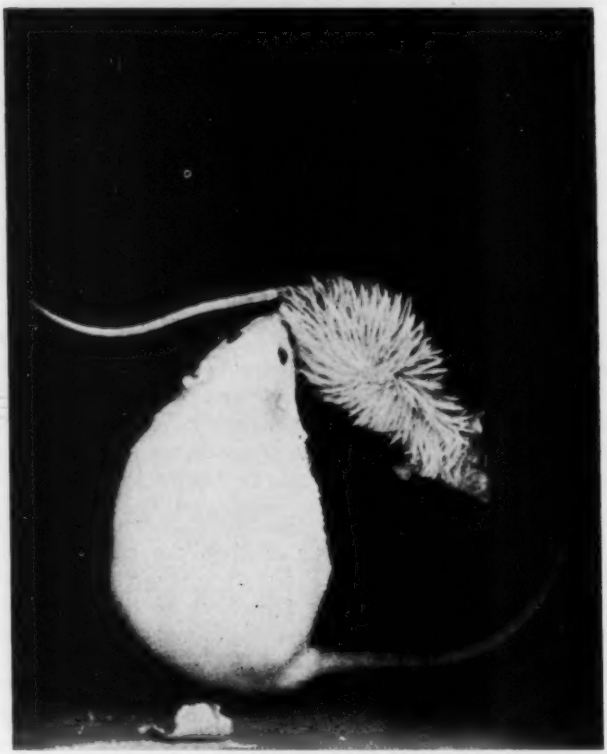

Fig. 7. The large control rat has received yeast throughout the experiment. The deficient rat is one of the "recovered" rats who was again deprived of the yeast for 29 days.

internal ear, may give misleading results due to artefacts, caused by improper fixation.

We have been limited to three methods of diagnosis: *1*. Diet, *2*. Laboratory tests, and *3*. Therapeutic tests. In addition to these, it would seem that the embryologic approach now enables us, by a study of a lesion in the eye, the ear, the

nose and the throat, to prescribe a vitamin which is known to have a preponderant effect upon a tissue, originating from one of the three germ layers. In the three previous methods of approach, we are aware of certain limitations. A study of the diet is not only laborious but by no means convincing, and at best leaves us with a very vague concept. The laboratory tests that are as yet available are highly specialized; and in most communities throughout the country such tests are not even available. Although a therapeutic test is naturally one of trial and error, yet it can be of definite help. In certain instances, a therapeutic test can be made by oral administration; but in order to form a reasonably sure conclusion as to any vitamin deficiency, one must look for a rather prompt response to the administration of a vitamin. This is best accomplished by injection; and six vitamins can now be so administered — (thiamin chloride, riboflavin, nicotinic acidamide, pyridoxine, ascorbic acid, and vitamin K).

The embryologic approach is definitely clinical. In our specialties we make an actual inspection of the "parts that can be seen"; and in addition, by tests such as a study of the visual fields, the vestibular and auditory tests, and the Elsberg measurements of the sense of smell, we secure accurate information concerning the "parts that cannot be seen."

One might say that, with the possible exception of the immortal soul, each one of us is simply a combination of derivatives from the original three germ layers. Consequently it is planned to investigate the effect on the three germ layers, by histopathologic studies in animals, of the *fetuses* of mothers that have been deprived of various vitamins. If this can be accomplished, it will provide precise information as to the preponderant effect of each vitamin on a germ layer. Such a study may also give us increased assurance in estimating the relation of the different vitamins to the derivatives from the three germ layers, and in prescribing the vitamins needed to cure lesions of the eye, ear, nose and throat.

REVIEW OF THE LITERATURE FOR 1940-1941.

In presenting these few abstracts from the mass of available literature, we have arranged them in the following order: General Survey and Comment; Vitamins and the Eye; Vitamins and the Ear, Nose and Throat; and then Vitamins in Relation to General Conditions, considering them in the order of "A," "B," "C," "D," "E," and "K."

GENERAL SURVEY AND COMMENT.

Since we realize that the present era is one of the use and also the abuse of vitamins, it is refreshing to quote the observation of Gordon:[3] "As we approach this subject we get a whiff of the odor of sanctity and a peep within the veil at what the world has come to think is the mystery of mysteries. Red flannel and goose grease had their day before focal infection was king, but now 'B_1' reigns in his stead. In spite of the pandemic hysteria about vitamins, there are definite values in the same public's recognition that it cannot live on quantity alone, nor upon quantity plus calories alone, and after this fitful fever they shall eat well."

Harris[4] emphasizes that there is a wide gap between the minimal diet (the amount needed to prevent well-defined clinical symptoms of deficiency) and the optimal (the amount needed to promote fullest health). It is generally agreed that upwards of 25 per cent of the population are unable to afford the cost of an optimal diet. The League of Nations Committee on Nutrition expressed this idea: "The evidence that inadequacy of diet is widespread is conclusive . . . the greatest single cause of malnutrition is poverty."

A significant resumé of our knowledge of the vitamins, and their own recent contributions to vitamin therapy are presented by Spies, Hightower and Hubbard.[5] Long after beriberi, rickets, scurvy and pellagra were recognized and described, the concept of nutritional deficiency diseases arose, and with the development of this concept a new chapter in medicine came into being. Considerable research has recently been directed toward the isolation and synthesis of so-called accessory food factors — known as vitamins. Some of these substances have been found effective in the treatment of beriberi, rickets, scurvy and pellagra. Following the brilliant investigations that led to the isolation, synthesis and clinical trial of thiamin, nicotinic acid, riboflavin, vitamin E, vita-

min B_6 and pantothenic acid, there came a period of confusion. The literature with regard to these vitamins, and to the deficiencies that arise from a suboptimal amount of them, is vast and often contradictory. Accordingly, the writers restricted their report to the present status of a few of the therapeutic advances made since 1936. "B_1" is of value in the treatment of beriberi and also of the acute neuropathy associated with chronic alcoholic addiction, pellagra and pregnancy. The isolation of nicotinic acid from liver concentrate marks a milestone in our progress in the study of pellagra. Lesions at the corners of the mouth were first described by Sebrell and Butler as a typical manifestation of riboflavin deficiency. Erosions around the eyes and a sharkskin appearance of the skin over the nose are also characteristic of a deficiency of this vitamin. Itching, burning and excessive dryness of the eyes, photophobia, granulation and extreme redness of the conjunctivae, particularly of the lower lids, are rather common complaints among persons suffering from riboflavin deficiency. The administration of riboflavin is followed by the disappearance of these lesions. Absorption of the fat-soluble vitamin K is dependent on the presence of bile in the intestine, rather than on the adequacy of "K" in the diet. Lowered prothrombin concentration may occur in conditions in which extensive intestinal lesions interfere with absorption or, more frequently, in conditions in which bile is excluded from the intestine by obstruction of the common bile duct. In such cases the administration of "K" will restore the normal prothrombin level. Bile salts, of course, must be given along with the orally administered vitamin in cases in which bile is not present in the intestine; otherwise the vitamin will not be absorbed. Recent work also indicates that newborn infants have a "K" deficiency the first few days of life and that the administration of "K" will prevent and cure the hemorrhagic diathesis in many cases of "hemorrhagic disease of the newborn." Pyridoxine (B_6): On the basis of the dramatic and beneficial effect of "B_6" in relieving muscular weakness and rigidity, an effort was made to determine whether a similar response would follow its administration to patients with Parkinson's syndrome — a severe lingering disease characterized by tremor of the extremities, weakness, delay of voluntary motion and muscular rigidity. Many more studies are necessary before conclusive statements can be made concerning the effect

of this vitamin. Vitamin E: For several years it was believed that "E" was concerned specifically with reproduction. During the past decade, however, a definite relationship between an inadequate intake of "E" and the normality of the cross striated musculature of the body has been established. Clinical studies of the therapeutic effect of "E" are still in the experimental stage. It is important to remember that single deficiency states seldom exist. This is not surprising, since the dietaries of persons in whom these diseases most frequently occur are deficient in many essential nutrients. The resultant clinical picture is extremely complex; frequently there is evidence of pellagra, beriberi, riboflavin deficiency, scurvy, "B_6" deficiency, "A" deficiency and anemia in the same patient. The diagnosis of one clinical deficiency syndrome, therefore, necessitates a thorough search for others. When treating persons with nutritional diseases, we should curtail their activities as much as possible, until restoration of the affected tissues is under way. Although each patient must be considered as an individual problem, there are certain general principles of therapy, applicable to all deficiency diseases. A well balanced diet of 4,500 calories, rich in protein, minerals and vitamins, should be eaten each day. Specific therapy, in the form of large doses of synthetic vitamins, induces more rapid and dramatic remission of symptoms of the specific deficiency diseases; shortens convalescence in the severe case; and assures more certain recovery. In the mild and moderately severe cases of mixed deficiency disease, dry powdered brewers yeast (from 75 to 100 gm.), liver extract (from 75 to 100 gm.) or wheat germ (150 gm.) should be given orally, as daily supplements to the diet. Yeast and wheat germ have an advantage over the pure chemical substances in that they contain nicotinic acid, "B_1," "B_2" and "B_6," as well as minerals, proteins, enzymes and salts — and probably still other as yet unknown but essential factors.

In a series of three articles, Wilbur[6,7,8] discusses vitamin therapy. Most of us are likely to think of vitamins as a group of substances related, perhaps physiologically, if not chemically, and as substances having very striking and at times miraculous effects. While they are entirely unrelated in chemical structure and differ widely in physiologic behavior, nevertheless all vitamins may be classed as catalysts. In essence, they are the sparks which motivate much of normal physiologic activity. This reference to "sparks" suggests very

clearly why vitamins are so essential, why they are needed in small quantities only, and why they do not serve as sources of energy or as material for growth and repair. The outstanding peculiarity of vitamin deficiency diseases is that they are entirely preventable and that, with the exception of a few extreme instances, they are completely curable. The important principles in the treatment of vitamin deficiency diseases are:

1. The use of an adequate, well balanced diet — high in vitamins, proteins, minerals and calories.

2. The use of supplements to the diet —

a. Concentrated and rich food sources of the vitamins — such as cod-liver oil, citrus fruit juices, yeast and wheat germ.

b. Concentrates of vitamins — including liver extract and proprietary preparations of concentrates.

c. Synthetic and crystalline preparations of vitamins — thiamin chloride, carotene, nicotinic acid, riboflavin, ascorbic acid and ergosterol.

3. The use of massive doses of vitamins in the early period of treatment.

The following diet has an approximate vitamin content of 20,000 units of "A," 580 of "B_1," 97 mg. of "C" and 1310 Sherman-Bourquin units of "B_2." The amounts vary depending on the vegetables, fruits and cereals selected; on the season of the year; and on the method of preparing the food. The addition of two tablespoonfuls of dried brewers yeast would increase the "B_1" content to approximately 1330 units; and the "B_2" content to approximately 1760 Sherman-Bourquin units.

TABLE 1.

BASIC OR FOUNDATION DIET.
(ADULT.)
DAILY QUANTITIES.

Milk	1 pint
Egg	1
Vegetables	3 large servings besides potatoes (one a green leafy vegetable)
Fruit	2 servings — one raw
Meat, fish or fowl	1 serving (about 4 oz.)
Butter	1 tablespoonful
Whole grain cereal and Whole grain bread	1 average serving 3 slices

The following diet has a higher vitamin content:

TABLE 2.

THERAPEUTIC DIET.

	Weight — Gms.	Average Servings
Milk	914	1 quart
Eggs	200	4
Lean meat (i.e., beef)	120	large serving
Butter	60	6 squares
Potatoes	150	large serving
Vegetables 5 or 10% (cooked)	100	average serving
5% (raw)	100	large serving
Fruit, stewed or canned	100	average serving
raw	100	average serving
Bread whole wheat	150	6 slices
Cereal cooked, Farina, dark	150	large serving
Dessert ice cream	200	2 average servings

To repeat, concentrated and rich food sources of the vitamins are the most useful forms in which the diet may be supplemented. These supplements include such substances as cod-liver oil, dried brewers yeast, wheat germ, butter, cream, and orange and other citrus fruit juices.

TABLE 3.

FOODS RICH IN VITAMINS.

Vitamin A	Butter, cream, egg yolk, carrots, green leafy and yellow vegetables.
Vitamin B	Whole grain cereals and bread, vegetables, potatoes, nuts, eggs, muscle and organ meats, milk.
Vitamin C	Oranges, lemons, grapefruit and their juices, tomatoes and tomato juice, raw cabbage, fresh strawberries, fresh fruits and vegetables.
Vitamin D	No adequate source. Egg yolk is richest food source.

Concentrates of vitamins include such materials as liver extract, fish-liver extract, fish-liver oils and a large variety of proprietary preparations of vitamin concentrates in the form of tablets, powders, capsules, pills and syrups. While such concentrates have the advantage of permitting administration of large amounts of vitamins in a relatively small

volume, they have the disadvantage of having been prepared, preserved or otherwise subjected to processes which may impair their vitamin content. Nevertheless they serve a very useful purpose if properly prescribed as a supplement to a suitable diet. The treatment of trigeminal neuralgia by "B_1" is still in the developmental stage; however, Borsook and others have already reported encouraging results. Such treatment, however, should continue over a long period, because favorable results may not appear for two or three months. As to "C," fresh orange juice contains about 40 to 60 mg. for each 100 cc. In scurvy, "C" in crystalline form may be administered by mouth or intravenously in doses of 300 to 1000 mg. daily. The average adult probably is saturated with "C" when 2000 to 3000 mg. is administered within a few days; therefore there is little advantage in giving doses larger than this. As healing occurs, the dosage may be gradually reduced. In occasional cases of scurvy a cure has resulted from giving only the proper foods; in occasional cases the disease has been cured only when the vitamin has been administered intravenously. In essence, prevention of "D" deficiency in infants depends upon giving "D" milk — (this contains 400 USP units per quart) — or the administration of 800 to 1000 units of "D" in the form of cod-liver oil, viosterol or other fish-liver oils. For the premature infant 1000 to 10,000 USP units may be necessary. Vitamin K: Deficiency of "K" may lead to a hemorrhagic tendency in certain patients with hepatic disease or in gastrointestinal conditions which interfere with intestinal absorption. The principal value of "K" is in its effect on the prevention and treatment of bleeding in cases in which the level of prothrombin in the blood is greatly diminished. Treatment of vitamin deficiencies of mild degree: For patients suspected of having an "A" deficiency of mild degree, doses of 25,000 to 50,000 USP units would be ample. With patients suspected of having a deficiency of the B Complex of mild degree, the diet supplemented with brewers yeast or wheat germ in amounts of 10 to 25 gm. daily, with or without thiamin chloride (5 to 10 mg.), nicotinic acid (100 to 300 mg.) and riboflavin (1 to 3 mg.) continued from one to three weeks should prove sufficient to relieve most of the symptoms and also to furnish an adequate therapeutic test to establish the diagnosis. For patients suspected of having a "C" deficiency of mild degree, a diet containing foods rich

in "C" can be supplemented by synthetic ascorbic acid in daily doses of 100 to 500 mg. for a period of two or three weeks. When in doubt as to the presence of a mild deficiency, if a physician elects to employ vitamin therapy he should make the keystone of his treatment a well balanced diet, rich in vitamins and calories. This diet may be supplemented with concentrates and synthetic products of vitamins in moderate doses; but it is much wiser to rely on foods rich in vitamins and on concentrates which contain vitamins in the natural form than it is to depend on "shotgun vitamin mixtures." The Councils on Pharmacy and Chemistry and on Foods, of the American Medical Association, recently have re-emphasized the disadvantages of indiscriminate use of preparations of this type. The Councils have accepted *none of them*. If significant improvement within a few weeks does not occur, vitamin therapy will probably prove disappointing, the diagnosis of vitamin deficiency may be questioned and the therapy discontinued. There is no advantage whatever in long-continued administration of large doses of vitamins to patients with vague complaints. In patients whose complaints are largely subjective and symptomatic, it is no more logical to expect results from vitamins than it is to expect continued good results and cure in treatment of all patients who have headaches with aspirin, of all who have coughs with codeine, or of all who have diarrhea with opium. The use of "E" in the form of wheat germ oil does not appear to have any value for the human being, with the possible exception of some cases of habitual and threatened abortion. There is no commonly accepted unit of "E." Synthetic substances such as alpha-tocopherol, are available for therapeutic use.

In a series of 1250 consecutive malnourished persons, Spies, Swain and Grant[9] studied predisposing causes, development, early diagnosis and specific therapy of nutritional diseases, during a period of time — February, 1938, to April, 1940. Clinical studies of these persons and analyses of their diets indicated a deficiency in calories, proteins, calcium, phosphorus, iron and the known vitamins. They had mixed rather than single deficiency diseases; and months and years of ill health have preceded the lesions. From the standpoint of practical application, mixed vitamin therapy is often desirable. The administration of the water-soluble vitamins,

together rather than individual — and of the fat-soluble, together rather than individual, has a definite usefulness in day to day treatment of the deficiency states.

Youmans[10] discusses vitamin therapy in clinical practice. Vitamins are normal substances required by the body to maintain health of tissues and all vital functions. Of themselves they have little or no action in the body, but nevertheless diseased processes occur when they are deficient or lacking. It is necessary to supply a normal amount of vitamins in order either to prevent or to correct a deficiency. Treatment with vitamins is of two kinds: Preventive treatment, to protect against a deficiency; and curative treatment to relieve a deficiency when it is present. A well diversified diet supplies all necessary food elements; and when possible, reliance should be placed on the natural food sources. Concentrates of natural food substances are next in order of importance. Substances closely related to food — such as yeast, fish oils and wheat germ are next in importance, and finally the pure vitamins themselves. At the present time great economic loss is occasioned by the use of *excessive* doses of pure vitamins — either because they are not needed or because they are continued beyond the time when other products and diet could be substituted. It may be highly advisable to administer nicotinic acid to a demented pellagrin, with ulceration in the mouth, and diarrhea — but such patients can usually receive relatively inexpensive concentrates — and then later on the proper foods. As to the individual vitamins: For protective doses of "A," the amount used should be in the neighborhood of 6000 to 8000 I.U. Doses up to 25,000 units may be used in severe cases. When there is difficulty in absorption or utilization of the vitamins, 100,000 to 500,000 I.U. daily must be used. For children, it is often advantageous to use preparations containing both "A" and "D"; but adults usually need little "D" and it is best to use "A" alone, or "A" in large doses and "D" in smaller doses. Carotene may be used instead of "A," but it is less readily absorbed and it is certainly not advisable when there is difficulty in absorption. Modern diets tend to be low in "B_1," and this vitamin is stored in the body in very small quantities. The daily requirements of "B_1" are about 1 mg. per day, being more in larger and more active individuals and less in smaller and less active persons. Growing

children require more "B_1" in proportion to their size. 1 mg. is equivalent to 333 I.U. This is an adequate daily dose for protection and also for the treatment of a mild deficiency. For severe deficiencies, such as polyneuritis and beriberi, 10 to 20 mg. daily are probably adequate. Products such as yeast or wheat germ are sufficiently concentrated for protective therapy and have the particular advantage of containing in addition other members of the B complex. Dried yeast furnishes 300 to 1,200 I.U. (or about 1 to 4 mg. of "B_1" per ounce). It is unnecessary to give large doses of "B_1" for more than a week or two. The vitamin itself can then be supplanted by yeast and a proper diet. Patients requiring curative treatment for pellagra receive nicotinic acid — which is the principal but not the sole vitamin concerned with this disease. For protective supplements yeast or concentrates of yeast, or similar substances, are best. Good brewers yeast in doses of an ounce a day will usually give protection. Nicotinic acid in 25 to 50 mg. doses is adequate for protection in most cases. For the curative treatment of pellagra or the more chronic deficiencies, nicotinic acid amide is better — in doses of 100 to 200 mg. daily. Nicotinic acid itself may cause erythema, itching, burning and sometimes nausea. The individual's tolerance for nicotinic acid is usually about 50 mg. When possible the amide should be given by mouth and in solution. Only a few cases of riboflavin ("B_2") deficiency alone are encountered. This deficiency is seen most often in association with pellagra. Riboflavin deficiency causes inflammation of the lips, with fissures at the corners of the mouth and seborrheic lesions about the nose. Yeast, yeast concentrates and similar preparations are often good sources of riboflavin. However, pure riboflavin can be given by mouth in doses of 2 to 5 mg. daily. When larger doses are needed parenteral administration must be used. Unfortunately, riboflavin is very unstable to light and solutions of it must be freshly prepared. Riboflavin is offered in combination with other vitamins, especially those of the B group, under the designation of "G" (expressed in terms of Sherman-Bourquin units). One Sherman-Bourquin unit equals about .003 of a mg. and if the daily need is 1 mg. of "G," then 400 Sherman-Bourquin units would be given. Many preparations contain 50 to 100 Sherman-Bourquin units per ounce — so the therapeutic dose would have to be excessively large. The indi-

cations for protective treatment of riboflavin deficiency are essentially the same as those in pellagra. "C" occasionally needs to be given in pure form as in cases of severe scurvy, or in patients allergic to fruits or vegetable juices. Protective or even curative treatment is best furnished by fruit and vegetable juices. These correspond to yeast and yeast concentrates for the B group, and to cod-liver oil for vitamins A and D. Orange juice ordinarily contains 0.5 mg. per cc. or 15 mg. per ounce. Therefore four ounces of orange juice a day will provide a protective or even curative dose of "C." Other fruits juices contain smaller amounts of the vitamin. When pure "C" is indicated, it can be given by mouth or if necessary by vein or intramuscularly. Repeated small doses are better than single large doses, because the level of "C" in the blood is not raised to such a high level all at once — and there is less loss through the kidneys. "C" in pure form is an acid and if given parenterally in large doses it must first be neutralized to avoid unfavorable local reactions. 200 to 300 mg. of the acid daily by mouth are usually sufficient for curative treatment. The pure vitamin need be used for only a few days. "D" is needed only occasionally in adults, although mild osteomalacia is more common than is generally suspected. This deficiency disease is partially due to a lack of sufficient "D" and partially to a lack of calcium. Youmans believes vitamins should be prescribed in adequate doses, expressed in proper units, and the amount estimated in body weight, if possible.

Miller[11] states that one hundred million dollars is spent annually in this country alone for vitamins and vitamin concentrates. Undoubtedly much of this money is wasted. For the present the physician must depend upon the patient's symptoms, general nutrition, certain physical signs, analysis of the diet, capacity of the patient to absorb and utilize vitamins — as criteria in prescribing them. For a few of the vitamins, particularly "C" and "K," more exact methods of determining the need are available. The need of the body for vitamins may be greatly increased in heightened metabolic states — such as hard work, prolonged fever, pregnancy, lactation and hyperthyroidism.

Siegel[12] has reviewed the work of 39 authors on the vitamins and their deficiencies with special reference to child-

hood. For many years in the past it was known that a deficient diet was responsible for typical clinical pictures: Ships' crews were provided with lime juice to prevent scurvy, and cod-liver oil was given to babies to prevent certain bone changes. The identification of vitamins, however, occurred within the professional life of many of us who are still young. So much enthusiasm was created by applying this new knowledge that it seemed a good field for commercial exploitation — and vitamins have been produced for sale in department stores and groceries. In spite of this the true value of these products has not been lost. Large amounts of carotene may pass through the placenta to the fetus. "A" also probably passes through the placenta, but the fetus may be able to form "A" from the carotene. Normal infants and older persons readily absorb carotene from the diet, but the rate of absorption is slower than the rate of absorption of "A" itself. A diet in which a nursing mother receives 75 units per kilogram of body weight per day is not only sufficient but is actually optimal. If the diet is sufficient the administration of "A" itself is superfluous, during lactation. Cow's milk shows seasonal changes in both carotene and "A" content. The seasonal changes in the carotene are greater than those in "A." A group of children had been living on restricted diets for periods varying from a few months to a few years; these children lost the alertness of health, and were listless and inattentive. Conjunctivitis was the most outstanding defect in this group. A study was made of the differential leukocyte counts of 157 subjects, whose diets and symptoms indicated a lack of "A." The characteristic changes were a mild leukopenia, a decrease in neutrophils, an increase in the number of large lymphocytes, with a corresponding drop in the small lymphocytes, the occurrence of degenerated cells and an increase in the number of immature cells. These findings suggest that the differential leukocyte count is of value in diagnosing a deficiency of "A" in man. Breast milk has been shown to contain less "B_1" than cow's milk. A large proportion of the infant mortality during the first year of life, which is associated with gastrointestinal disturbances, may be due to "B" deficiencies. As the result of an increased amount of "C" given to a group of infants during the first year of life, constipation was relieved in each instance of the 35 per cent of this series which manifested this symptom.

In the control group were 20 per cent who manifested constipation; these did not show a disappearance of constipation upon the use of the usual laxatives such as mineral oil and milk of magnesia. In another group of nursing infants who had failed to gain in weight because of insufficient breast milk, "B" was added to the diet of the mothers. Of these, 57 per cent were able to continue nursing their babies for periods varying from two to six months. Of this group of infants 50 per cent were constipated; the addition of the "B" to the diet of the mothers cleared up all but 5 per cent of the cases. In 100 older children it was found that 27 had anorexia, while 40 were constipated. These all received the proper diet and a special cereal, rich in "B." The appetite in each case was improved and the constipation was corrected. Spies, Walker and Woods, in studying 800 pellagrins, extended the studies to include the families of these patients. A diagnosis of pellagra was made in 194 children and six infants, and in each case the diagnosis was confirmed by therapeutic tests. It was often found that the diet of the mother was inadequate during pregnancy and lactation; and, as a result, the quality of her breast milk was poor and the supply often insufficient for the child's needs — so that the nursing infant had to be weaned soon after birth and then receive some sort of food which in many cases was inadequate for its nutritional needs. The response to treatment was as dramatic as it is in adults. The administration of nicotinic acid or yeast was followed by rapid improvement. The lesions characteristic of pellagra are seldom seen in infancy but frequently appear early in childhood. As to "C," it is now possible to determine the amount of it in the blood, the spinal fluid and the urine. While these tests are of value and interest, a diagnosis of scurvy cannot be made from the tests alone, because scurvy is a clinical entity. The fetus acts as a parasite and has higher levels of "C" than the maternal blood. As to "D," it seems that the principal factors in the reduction of rickets are artificial feeding and sunlight. Meyer considers that the protective "D" originates in the body of the child, under the influence of ultraviolet rays; and therefore that the specific prophylaxis and treatment of rickets may be achieved by irradiation. "D" is recommended also, especially in forms containing pure crystalline "D_2" in an oil. While there are advantages of simplicity and low cost, the

disadvantages are a possible toxic effect resulting from excessive doses; the permanent use of "D" in nonrachitic children may produce serious results. When cod-liver oil is used, only standardized preparations should be employed, both for prophylactic and therapeutic purposes. From 89 complete bioassays of human blood serum, an average "D" content of 116 U.S.P. units per 100 cc. was calculated. Cod-liver oil is the substance most frequently tested for "D" content. The average "D" content of medicinal cod-liver oil is rated as 10,000 to 15,000 units per 100 gm. It appears then that cod-liver oil has 100 times more "D" than human blood serum. The plasma prothrombin of the newborn infant can be significantly raised by feeding "K" concentrate to mothers, either for a prolonged period prior to delivery or during labor. The same result, but to a lesser degree, can be obtained by feeding "K" directly to the newborn infant.

VITAMINS AND THE EYE.

Kilgore[13] recognizes that many clinicians are at a loss to know when to prescribe vitamins, for what conditions, and why. From a survey of the literature and results obtained in his own practice, he concludes that their use is definitely indicated in ophthalmology. "A" is worthy of use in night-blindness, either actual or borderline; obstinate cases of low-grade chronic conjunctivitis associated with photophobia; blepharitis; and asthenopia failing to respond to refraction. "B_1" is of value in retrobulbar neuritis and toxic amblyopia; riboflavin in corneal conditions and perhaps in conjunction with "A" in night-blindness; "C" apparently has some effect on the optic media; and "D" may be of value in keratoconus and myopia.

Booher, Callison, Kline, Smith, Irish, Nelson and Daniel[14] state that, as early as 1500 B.C., the Egyptians and Chinese found that they could improve vision in dim light by eating generous amounts of the livers of animals. Over 3400 years later it has been learned that vitamin A is responsible for this improved visual adaptation, in those of course who had a deficiency in "A." There are at least five different substances found in foods that can supply "A." Soluble in fats, but scarcely soluble at all in water, four of these substances are yellow pigments. The fifth substance is vitamin A itself.

In a survey of the vitamins of the "B" group and their relation to ophthalmology, Veasey[15] recalls that, in 1914, it became known that the three main classes of cooked foodstuffs — proteins, carbohydrates and fats — plus the inorganic salts, were insufficient to maintain life. In that same year, Funk announced that certain diseases are due to a lack of specific substances — which he designated by the word "vitamins." It was later discovered that these substances fell into two main chemical groups: the fat-soluble and the water-soluble vitamins. The water-soluble group was termed vitamin B, and at that time was believed to be a chemical entity; later it was demonstrated that "B" is really a collection of substances of various chemical natures and biologic properties. Thiamin — "B_1" — is relatively heat resistant when dry; however it disintegrates rapidly at 100° C. when moist, especially in neutral or alkaline media. In the presence of acid it is much more thermostable. Thiamin is the only vitamin that contains sulphur. Riboflavin was first isolated in pure form from milk, and later synthesized. Its absence in rats leads to the formation of cataracts. In contradistinction to thiamin, it is heat-stable. It is now considered that riboflavin is present in all living cells. Nicotinic acid is a product of nicotine oxidation. Its presence appears to be necessary to prevent black-tongue in dog and pellagra in man. It is probable that other deficiencies are active in causing human pellagra. "B_6" is a white, crystalline substance which is thermostable. It has been definitely isolated, but has not yet been identified chemically. It is destroyed by sunlight and also by ultraviolet rays. The place that it occupies in human nutrition is not yet determined. The other components of the B Complex have not yet been isolated chemically and are known only by their effects on experimental animals. The best sources of thiamin and riboflavin are yeast, whole grains, wheat germ, beans, peas, lean pork, liver, kidneys, nuts, asparagus, parsnips, turnip greens, avocado, artichoke, egg yolk and dried prunes. The thiamin and riboflavin content of yeast varies with the species. In some forms of brewers yeast, the content is as high as 1,000 I.U. per oz. Wheat germ, an excellent source, contains somewhat less than 200 I.U. per oz. An avocado, for example, which is considered a relatively good source, contains about 14. Milk contains about 5 I.U. per oz. and butter 12 I.U. Yeast, liver

and kidney are especially rich in riboflavin — containing 10 times as much as other foods. Liver and kidney are relatively low in thiamin — with the exception of pig kidney, which has a good thiamin content. Chicken is a fair source of flavin. Egg-white is rich in riboflavin, but contains no thiamin and no nicotinic acid — which is abundant in fish muscle. The content of the other "B" factors is not known; but all yeasts are good sources of the whole B Complex. The yeast content in bread and beer, however, is not sufficient to add materially to the supply of this vitamin. Although nicotinic acid is a vitamin that prevents pellagra in man, thiamin, riboflavin and other factors may also be required. The chief dietary sources of nicotinic acid are meat, buttermilk, kale, green peas, tomatoes, turnip greens, wheat germ and yeast. Although the human requirements are unknown, the maintenance dose is over 200 mg. a week. Dosage of from 60 to 100 mg. daily for 10 days cures pellagra. Doses up to 500 mg. daily have been used, but toxic effects sometimes occur — flushing, burning, itching, and local heat in the skin. As to the "B" vitamins in ophthalmology: Fischer found thiamin in the normal lens, but states that it is present in cataractous lenses; that riboflavin is present in normal lenses; it decreases with advancing age; and is wholly absent in cataractous lenses. Yudkin considers that riboflavin is one of the essentials for lens health; and Van Heuven states that its presence is necessary for the conduction of light through the lens. Adler demonstrated the presence of flavin in the retinal pigment of fish, in a concentration 25 times greater than that found in the liver. It is only in the eye, in milk and in urine that free flavin is found. Bessey and Wolbach noted that corneal vascularization occurs in rats on riboflavin-deficient diets; on the administration of riboflavin the turbidity disappeared in two days and the vessels themselves in two weeks. They assert that a similar condition occurs in A avitaminosis. Yudkin described a more or less distinct type of sluggish corneal ulceration, resistant to or rendered worse by the usual therapeutic measures, which responds to "A" and "B." Koepcke also recommends "A" and "B" in the treatment of corneal ulcer. Many authors have reported the value of thiamin in herpetic keratitis. Experience with cataract in man is much less conclusive; there are no reports to show that individuals with cataracts are riboflavin deficient, and there is

nothing to demonstrate that riboflavin deficiency in the human species has an effect similar to that in the rat. From the clinical standpoint, there is much more evidence concerning the optic nerve; many case reports indicate that retrobulbar neuritis is not uncommon in B avitaminosis. As long ago as 1929, Shastid reported two cases of optic neuritis of undiscoverable etiology in which prompt remission of symptoms followed large doses of the B Complex. There is considerable evidence that toxic amblyopia occurs from the action of the poisons on optic nerves whose threshold has been lowered by the avitaminosis.

An interesting resumé of the history of night-blindness is given by Steffens, Bair and Sheard:[16] Although a disturbance of the sensitivity of the dark-adapted retina (night-blindness) was noted centuries ago, and although frequent observations of its association with malnutrition were made during the latter part of the nineteenth and the early years of the twentieth centuries, the etiology was not demonstrated until Holm, in 1925, demonstrated that rats became night-blind when fed for only a few weeks on a diet deficient in "A." This work of Holm was later verified by several investigators. Other experiments have demonstrated that retinas of frogs, rats and dogs suffering from severe lack of "A" are very low in visual purple. In the retinas of some, the visual purple was not present at all. Many investigations have shown that severe cases of night-blindness may be benefited or cured by adding "A" to the diet. So far as is known, "A" and its precursors are the only dietary constituents that will produce the curative results. Wald, in 1935, showed that "A" and the carotenoid retinene in the retina are chemically identical. Jeans and Zentmire, in 1934 and 1936, by means of an adaptometer, found a disturbance of dark adaptation in 21 per cent of a group of 213 children. Half of these children who showed low dark adaptation — and therefore relatively high values of threshold intensities, received a high-vitamin diet including cod-liver oil; after a period averaging 12 days, all of the children showed an improvement in dark adaptation.

Night-blindness is discussed by Isaacs, Jung and Ivy.[17] Night-blindness and other visual disturbances were recognized as due to impaired nutritional states by the ancient Egyptians and by Hippocrates. Night-blindness was found

to occur rarely except in periods of famine or war. In 1934, Jeans, Blanchard and Zentmire reported on its occurrence in Iowa school children. If one is to accept the increasing number of reports in the literature, poor dark adaptation due to subclinical "A" deficiency, occurs in approximately 40 to 50 per cent of the entire population. The authors' results with the adaptometer (Hecht) proved to be more reliable for the determination of visual dark adaptation thresholds than with the biophotometer. Twenty-eight normal young adults failed to develop recognizable signs of "A" deficiency when they received liquid petrolatum (5 cc. per kg. body weight) daily for 131 days. Twenty-nine normal young adults who did not receive the liquid petrolatum served as controls. Three subjects maintained on a diet averaging 74 U.S.P. units of "A" failed to show definite evidence of visual disturbances after 43 to 49 days. Doses of 300,000 units of "A" daily for as long as four months, in three individuals, failed to show harmful effects. The same amount occasionally failed to improve the dark thresholds in 10 patients suspected of an "A" deficiency.

McDonald and Adler[18] discuss the effect of anoxemia on dark adaptation of the normal, and of those who are deficient in "A." The tremendous increase in the sensitivity of the retina when it is kept in the dark for a prolonged period is common knowledge. It is also well known that certain pathologic conditions may affect this process of dark adaptation and give rise to varying degrees of night-blindness. Various metabolic disorders have been linked to an "A" deficiency by numerous investigators working in different fields. The recognition of "A" as one of the products of decomposition of visual purple when acted upon by light — and its rôle in the resynthesis of visual purple in the dark — showed rather conclusively that "A" is a factor in the chemical basis of vision. Hecht and Wald have made experiments under well controlled conditions and have shown that the rods and also the cones are affected in the deficient state. Wald has isolated iodopsin, or visual *violet*, from the cones; this is apparently analogous to the rhodopsin, or visual purple of the rods. However, there are other metabolic functions which are directly concerned with vision. One of the most important is an adequate supply of oxygen in the circulating blood. The changes produced by

anoxemia and "A" deficiency are dissimilar; this suggests that two different processes are involved in the visual response. This is further substantiated in that "A" deficiency does not alter the effect produced by oxygen lack. It is known that "A" is concerned with the photochemical basis of the visual response; and it is probable that anoxemia acts elsewhere in the visual system — on the nerve mechanism.

A review of the subject of "A," and a clinical survey of cases of asthenopia, apparently due to "A" deficiency, is presented by Cordes and Harrington.[19] Most of our knowledge of the vitamins has come from laboratory workers. The clinician often has a hazy idea of the subject. Yudkin defined vitamins as substances that are indispensable for the health and growth of all living cells. "Vitamins do not furnish energy, as do the proteins, fats and carbohydrates, but may be classified with the hormones and the inorganic elements — such as iodine, copper and manganese. These substances, according to some biochemists, may be looked upon as stimulating or conditioning agents of cell metabolism, perhaps as a type of biochemical catalyzer." "A" was originally called "fat-soluble A" by McCollum, its discoverer, because it occurs in cream, the fat of milk, and in the oil from the yolk of eggs. In this way he distinguished it from "B," which also occurred in milk and eggs — but was water-soluble. "A" is colorless, has been isolated in almost pure form, but has never been synthesized. In this country, avitaminosis A is usually in mild form. The symptoms of its deficiency are: *1.* Night-blindness (nyctalopia or hemeralopia), xerophthalmia, Bitot's spots and opaque whitish deposits in the scleral conjunctiva. These are the most characteristic signs of this deficiency. *2.* Keratinization of epithelial cells in various parts of the body. *3.* Cornification and eruption of the skin with papular and pustular lesions. *4.* Retarded growth, weakness and loss of weight. *5.* Increased suceptibility to infections of mucous membranes. It is generally accepted that in adults and older children, night-blindness is almost always the earliest sign of this deficiency. In fact, in this country the ocular manifestations of the deficiency are almost always limited to this early stage of night-blindness. "A" in our diet comes from two distinct sources: Carotene from the plant kingdom and true vitamin A from certain animal sources. The body is unable to

synthesize either. We must get it in our diet. No change takes place in either during the absorption process. "A" is stored directly in the liver, while carotene is converted into "A" before it is stored. It seems to matter little in the diet whether the vitamin present is in the form of "A" or carotene. Halibut-liver oil is the richest source of "A"; burbot-liver oil ranks next, followed by cod-liver oil and liver. Whole milk supplies more than any other single food, but large amounts are also found in butter, egg yolk and animal fats (beef and mutton). As to the provitamins, apricots are the richest plant source; large amounts are also found in spinach, carrots and chard. Smaller amounts (one-sixth as much as in butter) are found in green beans, green peas, Brussels sprouts, lettuce, tomato, yellow squash, sweet potato and pumpkin. Butter contains both "A" and carotene. Very little of the "A" content of food is lost in commercial canning or home cooking. It has long been known that the rods in the retina contain a purple matter — called visual purple or rhodopsin. This substance is very sensitive and becomes bleached and inactive when exposed to light. When the normal eye returns to darkness, this visual purple is very rapidly regenerated. Loss of the visual purple results in a loss of power in detecting faint sources of light. "A" has actually been found in the retina. The consensus of opinion at present is that "A" is picked out of the blood by the retina, presumably first by the pigment layer and later by the rods; and combines with protein to produce the visual purple. When exposed to light, this visual purple changes into visual yellow and retinene. This visual yellow, and perhaps the retinene, then change partly into "A" and partly into degradation products which pass out in the blood. The resultant "A" is then recombined with protein — and the process is again repeated. However, during this cycle a certain amount of these substances is lost. This necessitates a constant supply of "A" from the blood stream. As yet it is not understood how the bleaching of the visual purple sets up an impulse in the optic nerve. The writers report a review of 82 cases of persistent asthenopia in which they considered that "A" deficiency, as judged by the biophotometer, was the causative factor. These patients were treated with carotene in oil; the average dose was 30,000 units daily. Seventy-nine per cent of the patients obtained complete relief; 12 per cent obtained partial relief;

40 per cent of the cases were observed for a period of over six months, and 20 per cent between one and two years. After the usual causes of asthenopia have been corrected, the writers consider that a typical "A" deficiency is suggested by the following symptom-complex: Photophobia, associated with pain and rapid fatigue of the eyes upon use, especially at night. Difficulty in reading for longer than 15 to 20 minutes — with the print at times blurring momentarily. Headache and blurring, caused by driving an automobile or watching the movies. A chronic persistent conjunctivitis is a rather frequent finding. Often these symptoms are found to be associated with a deficiency in diet or a gastrointestinal disease, especially chronic colitis.

Fronimopoulos[20] studied a group of 41 subjects suffering from different types of keratoconjunctivitis allergica. "A" deficiency was found in a large number. This was demonstrated by a determination of "A" in the serum by Gaehtgens' method, and by testing dark adaptation by the Birsch-Hirschfeld photometer. There were no epithelial keratinized cells in smears from the conjunctiva. The ocular inflammation showed a definite tendency to recur as long as the "A" deficiency persisted. Statistics showed an increased occurrence of the disease in the spring of the year, and particularly in the years following the war.

During a series of studies on the cause and cure of night-blindness, Steven and Wald[21] undertook a field study in the region of Northern Newfoundland and Labrador. They state that beriberi is endemic in this area; and epidemics of night-blindness have occurred. Studies were made with a specially designed portable adaptometer and the threshold of the completely dark-adapted eye was measured. A rise of this threshold above a so-called "normal" was found to be inadequate as an index. Deficiency is reliably indicated by a vitamin A-labile threshold. This is one that, regardless of its initial level, is lowered at least 0.3 of a logarithmic unit, within two weeks of "A" supplementation. It is of interest that a threshold which reacted to "A," usually did so within one to six hours. In this field study, 9.7 per cent of the subjects were found to have a vitamin A-labile threshold; 3 per cent of the subjects showed clinical night-blindness. About one-half of those with A-labile thresholds were within "normal range."

About one-half of the subjects were also suffering from beriberi. Both "A" deficiency and beriberi are most prevalent in February and March. The "A" deficiency occurs in both sexes at an average age of about 26, and beriberi occurs mostly in males at an average age of 40. In subjects with both deficiencies, brewers yeast does not lower the threshold, while "A" alone is as effective as the combination of "A" and brewers yeast together.

Shettler, Bisbee and Goodenough[22] report the application of the biophotometer to the detection of "A" deficiency in workers engaged in matching the whiteness of porcelain used for electric ranges and refrigerators, in artificial light of an intensity 50 times the average light in schoolrooms, or 10 times that found in industrial inspection. Subjects showing "A" deficiency received 30,000 units of "A" daily, as carotene in oil, with a resulting improvement in biophotometer readings, greater eye comfort, improvement in general health, and better results in the matching tests.

According to Laval[23] the only decisive and definite uses so far established for vitamins in ophthalmology are: B Complex in cases of toxic amblyopia (alcohol or tobacco), and in optic neuritis associated with pellagra; and "A" in keratomalacia, xerophthalmia and associated ocular conditions. In 1931 the author became interested in the possible relationship between myopia and low "D" intake; by 1937 he was convinced that patients with myopia had not responded to treatment with calcium and "D." No matter how the question is approached, the myopic patient cannot be said to have suffered from a lack of "A" and "D" and calcium in infancy and childhood, nor is an increase in the intake of these substances capable of diminishing the myopia or keeping it stationary. There is experimental proof that "A" deficiency produces changes primarily in the cornea and sclera of experimental animals. There is insufficient proof that D avitaminosis by itself causes changes in the cornea and sclera. Children in New York City from both poor and well-to-do homes get sufficient amounts of "A" and "D" in their diets. Excessive doses of viosterol have caused pathologic changes in children, and in adults may be carcinogenic in effect. Myopic persons should not always wear their corrections for distant vision unless it is absolutely necessary, but they should always wear their glasses for close work.

Redding[24] states that phlyctenular disease is one condition which has practically disappeared in America in recent years. It was formerly one of the most frequently seen diseases of the eye. It affects either the conjunctiva or cornea, or both at the same time. It may be manifested by a slight redness of the conjunctiva or an ulcer. When the cornea is involved there may be a slight redness of the corneoscleral junction or a deep ulcer. This condition has been called conjunctivitis eczematosa, and again scrofula. Since time immemorial, tuberculosis has been considered to be the cause. Lately allergy has been suggested as the causative agent. This condition is one of childhood, occurring between the ages of 2 and 10 years. If not treated properly, it becomes very resistant. These children suffered from photophobia, iritis and blepharospasm. These eye conditions used to be very common following epidemics of measles. Another distinct type of phlyctenular disease received the name scrofula. The glands of the face and neck were swollen; sometimes there was suppuration. The tuberculin test was often positive — as it was also in many healthy children. Some authors called it tuberculosis — and so it remains in textbooks up to this day. During the past 10 years, not a single case of phlyctenular disease among children has been seen at any of the state tuberculosis sanatoria. Several years ago, Redding noticed a falling off of the number of cases of phlyctenular disease in his office and hospital practices. He then began to gather statistics from many United States hospitals and some of the hospitals of Europe. There was a sharp drop in the number of cases in all of the United States hospitals and the year in which this drop appeared was about the same in each instance. The European statistics show exactly the opposite results. Instead of a drop in the number of cases of phlyctenular disease, there was a rise. At this time the only possible explanation for the dropping off of the cases in the United States seemed to be the diet. Redding therefore wrote a letter to one of the largest chain grocery stores in this country, inquiring about the consumption of fresh fruits and vegetables. In reply to his inquiry it was found that about 1923, green vegetables and fresh fruits suddenly became necessary commodities to the consumer. They became somewhat *nonseasonal* in distribution during the period from 1922 to 1924. It was in 1923 that the volume began to attain large proportions; about this time or a year

later the chain stores began adding these commodities in a big way and introducing them at prices appealing to consumers, who began to buy and consume these products on a larger scale than at any previous time. The one thing that these foods contain in greatest abundance is vitamin A. It was about 1923 that the use of cod-liver oil in the diet in childhood became almost universal. The poorest family was able to afford fresh fruits and vegetables because of the improved refrigeration for distance shipping. Conditions were not the same in Europe. The refrigeration conditions were not the same; in fact, refrigeration was not used to any great extent. The children of the poor subsisted on the bare necessities of life. Experimental studies on "A" deficient rats revealed that the phlyctenular disease so produced was identical to that in the human. Redding then started to treat his patients with large doses of cod-liver oil. Fifteen cases improved in a few days and all of them recovered completely in 10 days. During the past three years, Redding has seen only three cases of phlyctenular disease. These were in children with poor eating habits. After a change of diet their conditions cleared up promptly. Thus during the past decade the most prevalent eye disease in the United States has disappeared. If the same feeding habits had been followed in Europe, similar conditions no doubt would have resulted.

Fischer[25] states that the "B_1" content of the lens is .001 microgram; a cataractous lens contains no "B_1." In 10 cataractous lenses there was an increase in pyruvic acid. A group of 12 cataractous lenses showed a greater increase in pyruvic acid content for very dense cataracts. The author believes that faulty metabolism of the glucosides is an important rôle in the pathogenesis of cataracts.

Ocular conditions associated with clinical "B_2" deficiency are discussed by Johnson and Eckardt.[26] *1.* In 1931, Day, Langston and O'Brien described cataract resulting from a deficiency of "B_2" in young rats. No correlation has been made between the type of change in the rats' eyes and the changes in cataract in the human being, as determined by the slit lamp. It is improbable that we will encounter a lack of "B_2" in the human being, to the extent necessary to produce cataract. Although conclusive evidence is not yet available, patients with cataracts should receive a plentiful amount of

"B_2." *2.* The writers call attention to the work of Kruse, Sydenstricker, Sebrell and Cleckley on the use of "B_2" in interstitial keratitis, in two cases. In each case a decrease in the opacity was evident after giving "B_2" — in one instance three weeks later and in the other, two and a half months later. *3.* At the University Hospitals of Cleveland, the writers gave "B_2" and the B Complex for interstitial keratitis; they report that the results have not been spectacular. *4.* In cases of rosacea keratitis, the writers have found "B_2" of sufficient value to cause them to discontinue the usual practice of cauterizing the cornea. *5.* In 1940, Sebrell discussed a probable relationship in pellagrins, between "B_2" and eye lesions, such as inflammation of the cornea, corneal ulcers and opacities.

Sydenstricker[27] is of the opinion that riboflavin deficiency manifested by early ocular signs offers a method for the diagnosis of B Complex deficiencies at a stage when no gross signs are present. A deficiency in riboflavin is characterized by photophobia and dimness of vision, at a distance and in dim light; cheilosis, and a specific type of glossitis. The earliest and most constant finding is a superficial vascularization of the cornea which may progress to a severe interstitial keratitis. In five cases iritis accompanied by keratitis and cheilosis subsided after treatment with riboflavin. Abnormal pigmentation of the iris was seen to disappear with riboflavin. Under experimental conditions 5 mg. of the vitamin daily has been used as the average dose. When there was evidence of poor intestinal absorption this has been increased to 10 or 15 mg. by mouth; 3 mg. daily with adequate diet is sufficient for the cure and maintenance of the majority of patients. In extremely depleted cases with polyavitaminosis, 10 mg. daily of riboflavin-sodium has been given intravenously.

Clements and Searcy[28] use cod-liver oil as an adjunct to the usual treatment of blepharitis, persistent simple conjunctivitis, phlyctenular conjunctivitis, hordeolum, and any disease of the eye involving the cornea, vitreous, choroid or retina. In addition, they instruct the patient to eat more green vegetables and more of the foods that contain yellow pigment, notably bananas, carrots, yellow sweet potatoes and butter. They recently treated four cases of dendritic keratitis in which the corneal lesions were healed within two weeks. Treatment consisted of one drop of 1 per cent atropine solu-

tion administered at the time of the first office visit, and two teaspoonfuls of cod-liver oil three or four times daily at home.

Knapp[29] studied a large series of patients, since 1933, and concludes that a disturbance in the vitamin D-calcium-phosphorus metabolism is concerned in the etiology of myopia. In the presence of a calcium imbalance, there may be a weakening of the fibrous tunic, which may give rise to myopia. Once a condition of progressive myopia has been established, treatment with the vitamin D Complex is indicated. The myopic eyes that respond to this therapy may undergo an actual shrinkage of the globe. For the prevention of the onset of myopia, the vitamin D Complex probably has another field of usefulness. Given a patient showing a diminishing degree of hyperopia, and one who is approaching the axial myopia side, it might be well to fortify his diet with vitamin D and calcium.

VITAMINS AND THE EAR, NOSE AND THROAT.

Canfield[30] comments on vitamin therapy for deafness. Some fairly well-controlled experiments seem to warrant our attention to this subject. Experimental evidence with certain nerves indicate that damage caused by vitamin deficiency can be overcome by the therapeutic use of these substances. It is now supposed that there is a pathologic stage in the cochlear mechanism in which the nerve elements lose part of their function without irreparable damage. Enough people now have improved hearing following the administration of the B Complex, so that it must be considered as part of the therapeutic armamentarium of the physician at this stage of the experimental approach. In experimental animals, a stage of cloudy swelling in the cochlear ganglia has been observed which may very well be eliminated by a proper diet. This cloudy swelling doubtless accounts for some partial diminution in nerve function, and if the deafness can be treated at this stage with adequate diet, it is believed that the function will return. There are those who believe that prolonged treatment will even result in repair of the nerve which has gone beyond the cloudy swelling stage.

Alfoldy[31] finds that administration of "B_1" in cases of hyperesthesia of the VIII Nerve of different causes, appeared to relieve tinnitus; the effect on hearing was very uncertain.

Baer[32] reports negative results obtained in 15 cases of otosclerosis with a combined "B_1" and "C" therapy aiming at vitamin C saturation. Preliminary tests for "C" deficiency were made. A general "C" deficiency varying between 600 and 1,500 mg. was found. Vitamin treatment was preceded by air insufflation, ear massage and diathermy, lasting for weeks; this was followed by the peroral use of "B_1" and the B Complex, and by simultaneous intravenous injections of "C" (once or twice a week). Both vitamins were administered for from two to three months. Though no improvement in hearing was achieved, there was a relief of headache and a cessation of noises in the ear.

Szolnoky[33] studied the results of "C" therapy in five cases of internal ear deafness and tinnitus, and of five patients with chronic otitis media. In all 10 the hearing was markedly impaired. All of these patients complained of tinnitus. This was diminished by the injection of "C." Five other patients with otosclerosis also received injections of "C" and the tinnitus diminished — although there was no improvement in the hearing. Apparently otosclerosis has no relationship to hypovitaminosis. Among 40 patients with nerve deafness, 30 were otosclerotics, eight were luetics, one "senile," three had neuritis, four exhibited only the symptoms of tinnitus, and two had occupational deafness. The loss of hearing of arteriosclerotics is attributed by Politzer and Mortugo to a degeneration of the wall of the internal auditory artery. Alexander substantiated their histologic findings, but in addition found atrophy of the papilla acoustica, and a degeneration of the fibers of the cochlear nerve. In arteriosclerotics the outstanding symptoms of ear disease are dizziness, tinnitus and deafness. When these occur in a young individual the cause is usually syphilis. Eight cases out of 30 had a positive Wassermann. "C" proved of value even in some of these syphilitic cases. For the four patients who exhibited only tinnitus, "C" therapy proved of some value — although at least some of this improvement probably resulted from mere suggestion. In uncomplicated arteriosclerotic patients suffering from deafness and tinnitus, "C" therapy proved of considerable value. No improvement in hearing resulted in the patient with "senile" deafness. Throughout these experiments, a check was made on the amount of "C" in the urine and in the blood.

Griebel[34] observed the effect of vitamin therapy in severe cases of laryngeal tuberculosis with numerous ulcers, perichondritis, mucous membrane erosions of the throat, etc. In order to study the experimental as well as the clinical results, he deprived guinea pigs of "B" and later sprayed the throats with tubercle bacilli. Guinea pigs deprived of "B" over a long period of time and then infected in this way, all showed changes in the mucous membrane of the mouth, tongue and throat. Control guinea pigs on a normal and full diet received similar sprays of the bacilli; the mucous membrane of the pharynx and larynx was unaffected and remained normal. Of the 28 severely ill patients which received "Redoxon" and "Benerva," 16 showed no remaining ulcers of the larynx; five died of pulmonary tuberculosis; and seven showed some relief of dysphagia. One patient who had been on this therapy for 14 days died. He previously had had numerous ulcerations on the pharynx, on the left tonsil and also on the posterior wall of the larynx. Histologic sections revealed no evidence of ulcerations in the areas previously affected, which had shown definite lesions prior to the vitamin therapy. Another patient with ulcerative laryngeal tuberculosis and dysphagia had lost 20 lbs. in four weeks; after six "Redoxon" injections he gained 2½ kg. in 10 days, ulcerations on the epiglottis had disappeared, and the posterior wall of the larynx showed no lesions. The mucous membrane ulcerations of tuberculosis seem to respond to "B" therapy.

Winans[35] points out that in "B_1" deficiency the evidence of peripheral neuritis is well known. In the past few years, several patients have been observed in which another striking symptom has been noted — a change in the character of the voice. Osler quoted Antonio Sison as one of the early observers of difficulty with the voice in beriberi; Loeb and Greenebaum have recently reported a case of beriberi in which the voice was reduced to a whisper; and Winans and Perry, in 1936, reported cases of beriberi in which the change of voice is one of the symptoms. The change of voice may escape notice, because of the natural assumption that weakness of the voice is simply a part of the general weakness that these patients present. However the change is not purely a weakness but rather an actual alteration in the pitch and character, as well as the strength of the voice sounds. Occa-

sionally phonation is reduced to a whisper. The usual alteration has been from the normal adult sounds to the thin and piping type of childhood. It is believed to be caused by neuritis of the laryngeal branches of the X Nerve. Laryngoscopy has not been productive of much information, except in advanced cases of bilateral abductor paralysis. One ambulatory patient consulted several laryngologists for fatigue and huskiness, before she was relieved by the administration of "B_1." In these cases the pulse rate was never under 90 and was usually over 100. This change of voice seemed to improve independently of the improvement of the patient's general condition. In this series the symptom was found only in women. Perhaps this is a coincidence, since more women than men with the findings of "B_1" deficiency were observed on this medical service. However, several men were observed who were fully as ill, and who presented as complete evidence of polyneuritis as the women — but without any alteration of the voice. It would seem that a change in the voice is one of the symptoms of "B_1" deficiency; and the detection of this symptom may provide a clue to or confirmation of the diagnosis of this deficiency.

VITAMINS IN RELATION TO GENERAL CONDITIONS.

"A"

The localization of "A" in the body has been studied by Popper.[36] He points out that it is distributed throughout the entire body, whether animal or human. Chemically it is a long alcohol chain. It appears that there is a close connection between "A" and the body lipoids. The study of "A" deficiency, however, gives a different impression as to the site of the effect of this vitamin and its rôle in the organism. Vitamin A deficiency is characterized as an affection of the epithelium — even though its location in the body is in entirely different structures. The lack of "A" produces an atrophy in the epithelium — followed by a reparative proliferation of the basal cell layer. This newly formed product differentiates into a stratified keratinizing epithelium, independent of its original structure. Typical eye changes, xerophthalmia and keratomalacia, are due to such a metaplasia of the epithelium. These changes appear very late. One of the earliest manifestations occurs in the skin. The growth of the

teeth is altered early, due to epithelial changes of the enamel-forming organ. The enamel formation stops and the dentine formation decreases — thus leading to deformities of the teeth. The respiratory epithelium reveals similar alterations. Plugging of the small bronchioles occurs; this may be the cause of the pneumonia which occurs in poorly nourished children. All this leads to the conclusion that the absence of "A" induces proliferative growth of the epithelium. There is however one phenomenon in "A" deficiency which is not primarily related to such proliferative growth, namely night-blindness — in which the regeneration of the visual purple is disturbed, and dark adaptation is impaired. Night-blindness is one of the first signs of a lack of "A"; and the examination for dark adaptation is the most widely used clinical test for "A" deficiency at the present time. Popper observed, by means of the fluorescent microscope, the distribution of "A" in the liver, intestines, adrenals, ovaries, testicles and other organs of rats and humans. The endothelial cells of the liver and kidneys are the last cells in the parenchymatous organs to lose this vitamin. The retina never loses it completely. For vision, high amounts of "A" in the retina are necessary; and it does not completely disappear from the retina even in extreme "A" deficiencies. "A" also plays a part in the production of sex hormones. Normally this vitamin is stored chiefly in the Kupffer cells of the liver and in the fat under the skin and throughout the body.

Comments on "A" deficiency and a case report are given by Stone and Courtney.[37] The characteristic pathologic changes are found in many structures. First there is an atrophy of the epithelium; then a reparative proliferation of the basal cells and differentiation of the new product into a stratified keratinizing epithelium. The replacement epithelium is identical in all locations, and comparable in all its layers with epidermis. In human infants such keratinization has been found in the conjunctiva, cornea, mucosa of the nares, accessory sinuses, trachea, bronchi, pancreas, renal pelves, ureters, salivary glands, uterus and periurethral glands. The commonest and earliest appearance of such metaplasia is in the trachea and bronchi. This early effect of an "A" deficiency upon the respiratory mucosa is thought to be a satisfactory explanation of the frequency, severity and persistence of the pneu-

monias that have been in so many instances responsible for the deaths of infants. The involvement of the eye occurs late. The case report of a baby who received an adequate amount of "A" but was unable to utilize it: In brief, keratomalacia and xerophthalmia developed in an infant who, although he was receiving an adequate amount of "A," was unable to utilize it. Autopsy showed an obstructive biliary cirrhosis. It is believed that the absence or deficiency of bile in the intestinal tract interfered with the normal digestion of fats and prevented the absorption of "A" to such a degree as to bring about the keratomalacia and xerophthalmia characteristic of a gross deficiency of this vitamin.

McDonald[38] states that the average daily requirement of "A" for adults is 2000 to 3000 I.U.; and a daily diet comprising 500 cc. of milk, one egg, 25 gm. of butter and one serving of greens meets this requirement. In pregnancy, and in illness, at least 5000 units should be supplied daily. Six thousand to 8000 are ample for a normal growing child. If preparations containing both "A" and "D" are given in large doses, they may cause an annoying feeling of fullness. For this reason unless "D" is also needed, it is better to prescribe "A" alone. It is seldom necessary to prescribe more than 10,000 units of "A" daily.

In an institution for pulmonary tuberculosis, Harris and Harter[39] are led to believe that practically all tuberculous individuals are deficient in "A." It is not known whether a lack of "A" is a causative factor in tuberculosis or whether tuberculosis produces a deficiency in "A." Large doses of halibut-liver oil may be necessary for these patients, but the writers have used only 30,000 units daily for a period of four weeks. Fifty or more years ago pulmonary tuberculosis was treated with cod-liver oil; and our confreres even at that time were positive that it helped in no uncertain way.

"B"

The B Complex in human nutrition is discussed by Elvehjem.[40] Some of the most interesting findings have been made with this particular group of vitamins. Perhaps for two reasons — first, the chemical structure of water-soluble vitamins is far more complicated than that of the fat-soluble vitamins.

"B_1" was first synthesized in 1936, and we have seen an average of one B vitamin synthesized each year since that time. Second, because the B vitamins are part of the complicated enzyme system; and the work on the relation of these vitamins to metabolism has not only aided us in understanding their function, but in many cases has also helped us to understand the intricacies of metabolism itself.

Jolliffe[41] has summarized the more recent discoveries relating to vitamins of the B Complex. He believes that if the knowledge now available be applied to the prevention and treatment of human disease, important strides will be made. The vitamin B Complex is known to consist of at least a dozen fractions. Only five of these are available in crystalline form for clinical use. The neuresthenic syndrome is probably the most common manifestation of "B_1" deficiency. To be sure, not all neurasthenia is caused by thiamin deficiency. If the triad of anorexia, fatigue and insomnia is not relieved, other neuresthenic symptoms develop. The central nervous system manifestations of "B_1" deficiency occur after peripheral polyneuropathy is evident, and are a part of Wernicke's syndrome. Oculomotor palsies of this syndrome respond to "B_1" therapy. The stupor also responds, but the ataxia is not affected. Williams, Mason, Wilder and Smith noted in subjects with "B_1" deficiency, abnormalities that could be demonstrated by the electrocardiograph. The addition of "B_1" to the diet resulted in normal electrocardiograms. Jolliffe and his co-workers noted precordial pain and electrocardiograph abnormalities in experimental subjects. In persons past middle age, the coronary arteries may be unjustly condemned because of precordial pain and abnormalities in the electrocardiogram. Clinical knowledge of riboflavin deficiency dates back to December, 1938, when Sebrell and Butler described the lesions resulting in women maintained on the diet of Goldberger and Tanner. There was a pallor of the mucosa of the lips followed by maceration — superficial transverse fissures appeared bilaterally. Simultaneously, the lips became red along the line of closure. There was fine scaly desquamation in the nasolabial folds, alae nasi, in the vestibule of the nose, and on the ears. Keratitis has also been associated with these signs of "B_2" deficiency. Jolliffe and his co-workers have reported on riboflavin deficiency in 15

patients. Thirteen also had nicotinic acid deficiency, seven "B_1" deficiency and three "C" deficiency. One showed no evidence of another deficiency. The facial lesions in these 15 patients consisted of filiform excrescences of seborrheic nature sparsely scattered over the face. These filiform lesions resembled urea frost. In addition, the patients showed fissures and macerations at the angles of the mouth. The lips, particularly the lower, frequently showed a marked increase of vertical fissures. The vestibule of the nose was affected with similar lesions. In these patients, the lesions could be controlled by administration of synthetic riboflavin; and the lesions would appear again when the patients received a diet poor in B Complex. The lesions were not relieved by "B_1" or nicotinic acid therapy. Partial chronic nicotinic acid deficiency causes scarlet-red stomatitis, glossitis, diarrhea, bilateral symmetrical dermatitis and mental aberrations. These signs and symptoms may occur alone or in any possible combination. Stomatitis is too frequently considered to be due only to Vincent's infection. Hence vitamin therapy is neglected. Nicotinic acid therapy results in blanching of the stomatitis within 24 to 48 hours, and the Vincent's infection heals without general or local therapy. Jolliffe and his co-workers have reported 150 cases of an encephalopathic syndrome. This syndrome may occur alone, or in association with pellagra, symptoms of "B_1" deficiency, oculomotor disturbance of Wernicke's syndrome, or scurvy. The clinical picture of this encephalopathic syndrome is one of clouding of consciousness, cog-wheel rigidities of the extremities and uncontrollable grasping and sucking reflexes. The mortality for this syndrome was almost 100 per cent — and has been reduced to 15 per cent, by the use of nicotinic acid. It has been suggested that "B_6" may be concerned with muscle metabolism. Spies, Bean and Ashe described a syndrome characterized by nervousness, insomnia, irritability, abdominal pain and difficulty in walking. Following the intravenous administration of "B_6" these signs and symptoms disappeared. Jolliffe has accumulated evidence that "B_6" plays some part in the control of adolescent acne. The author selected 15 patients having paralysis agitans and gave to each 50 to 100 mg. of "B_6" daily. Four showed definite improvement and two were subjectively improved. Recently he has treated 40 patients with paralysis agitans; 20 per

cent were definitely improved by intravenous injections of "B_6." The rigidity and weakness of paralysis agitans respond to "B_6" favorably. It is not surprising that with our newer knowledge of nutrition, the necessity for restoring vitamins and minerals to foods should receive attention. A recent editorial in the Journal of the American Medical Association pointed out that England has fortified margarine with "A," and flour with calcium and "B_1" — in an effort to maintain at high levels the strength and growth of its people. Stiebeling and Phipard show the diets of wage earners and clerical workers to be inadequate in both vitamins and minerals. Sebrell believes that nutritional diseases are our greatest medical and public health problem. At the present time, the diet of the American contains 650 calories, derived from wheat flour — practically free from vitamins and iron; and an equal number of vitamin-free calories from sugar. These sources provide about 50 I.U. of "B_1." In A.D. 1840, the same number of calories in the same substances used to provide at least 600 I.U. of "B_1" and also other B vitamins. Since 1840, the consumption of wheat flour has diminished, and the vitamin and mineral content of the wheat has been diminished even more — due to refinement in the milling methods. In addition there has been a marked increase in sugar consumption and at least a two-thirds reduction of the vitamin B consumption by the American people. Each pound of flour would have to contain 1.66 mg. "B_1," 1.2 mg. "B_2," 10 mg. nicotinic acid, 20 mg. iron and 175 mg. calcium — if it is to be restored to the vitamin and mineral levels of the flour used a century ago. Bread made from restored flours has a slightly creamy color and a wheaty taste. It may be that a baker's yeast will be grown that will contain unusual amounts of thiamin, nicotinic acid and riboflavin, so that it will be necessary to add to the flour only "D" and the minerals.

Elsom[42] discusses the remarkable strides in our understanding of "B" deficiency since 1933. At that time it was fantastic to believe that "B" was lacking in the food because its wide distribution in common foods was already beginning to be recognized. At the Philadelphia General Hospital, a series of clinical experiments were conducted on B Complex deficiencies. A study was made of normal individuals whose diets were adequate in all requirements except the B Complex.

These patients were observed over periods varying from three months to one year; a mild B Complex deficiency developed. First of all there was a loss in weight, followed by edema. The earliest symptoms were fatigue and anorexia. Mental depression, apprehension, fearfulness and inability to carry through a logical train of thought were characteristic of the mental symptoms. In order to study the effect of synthetic preparations of the B Complex upon these deficiencies, certain patients received "B_1." In one instance, when the weight began to decline, this vitamin was given and a temporary increase in weight resulted. The dose of "B_1" was then trebled; in spite of this the weight began to decline. After this a source of the B_2 Complex was given and again a temporary increase occurred. The dose of the B_2 Complex was then trebled, without effect. It was not until the patient received brewers yeast that the weight returned to normal and was retained. Another patient received 15 mg. of "B_1" daily and a temporary increase in weight resulted. The dose of "B_1" was then trebled, with no resulting change in weight. Riboflavin was added to the diet with a temporary increase in weight. In this way Elsom has shown the incomplete effects of "B_1," "B_2" and nicotinic acid on the manifestations of *B Complex* deficiencies. These three factors slightly relieved more than one-fourth of the typical manifestations. Brewers yeast was required to relieve the remaining three-fourths of the symptoms. It is probable that undesirable clinical situations will result from the use of separate synthetic vitamins to the exclusion of others. Elsom believes that unless there is an urgent indication for the use of vitamins parenterally, as in the pernicious vomiting of pregnancy, they should be given by mouth. Because of their high vitamin requirements, children are most susceptible to variations in the diet and synthetic vitamins are of help in such conditions.

Drazin[43] illustrates the beneficial effects of vitamins of the B Complex in the treatment of three cases. Case 1 was a white man, age 60, operated on for hypertrophied prostate. He was discharged from the hospital with an abdominal sinus. About one month later he was readmitted with the diagnosis of pellagra, complicated by the persistent sinus. He received 500 mgs. of nicotinic acid and a 4,000 calorie, high protein diet. At the end of two months the pellagra

symptoms had disappeared. Case 2 was a man, age 43, with a history of rheumatic heart disease for 16 years. He had consumed very little food at home and on admission to the hospital showed a thiamin chloride deficiency. He had a bilateral peripheral neuritis involving the lower extremities with no knee and ankle jerks. There was edema of the feet and legs and a right hydrothorax. The heart was enlarged. He was mentally confused and suffered from hallucinations and delusions. Fifty mg. of thiamin chloride was given intravenously, and within 24 hours he was mentally clear. This dose was continued for five days — then 25 mgs. for two days, followed by 10 mgs. for 10 days, and finally 5 mgs. daily. Considerable of the edema subsided and there was less hydrothorax. Although he died, due to heart failure, there was nevertheless a definite response on the part of the patient to the thiamin chloride. Case 3 was a man, age 23, with extensive pulmonary tuberculosis. A thoracoplasty had been done. He was emaciated and the tongue as well as the mucous membrane of the mouth showed grayish white sloughs with areas of deep red between. Swallowing was very painful. Muscles were atrophic and tender. He received 3600 mgs. of nicotinic acid over a 10 day period; and then 50 mgs. daily for two weeks. It was then discontinued because he developed symptoms of intolerance. Two weeks later it was resumed in 50 mg. doses. He received, in addition, a high protein, high caloric diet and other vitamins. After several months he had recovered sufficiently to be discharged. The mouth symptoms disappeared and he gained in weight.

Induced thiamin deficiency in man was studied by Williams, Mason, Wilder and Smith.[44] In a previous study a report was made on the effects of depriving four young women of thiamin in their diet for 21 days. The present study is of a similar nature except that autoclaved yeast was given instead of crystalline riboflavin and nicotinic acid. Six white women were selected, ranging in age from 21 to 46 years. They received a basal diet which did not provide more than 150 micrograms of thiamin daily over a period of 88 days. This was the length of time the diet could be tolerated during the winter months. It was tolerated for 147 days by four subjects who received it during the summer months. The more active subjects experienced symptoms earlier than

the less active. The symptoms differed from classic beriberi, because edema, cardiac dilatation and peripheral pain were absent. In the early stages the symptoms closely resembled neurasthenia and the later stages, anorexia nervosa.

Dolger, Ellenberg and Pollack[45] studied the urinary excretion of "B_1" active substances in a patient with chronic alcoholism, peripheral neuropathy, and pulmonary tuberculosis. The method used was developed by Schultz, Atkins and Fry. Following the second intravenous injection of thiamin hydrochloride (100 mg.) only 7 mg. of "B_1" active substances were recovered in the urine. On succeeding days the response to 100 mg. of intravenous "B_1" daily, increased to 80 per cent in the urine. Treatment with large doses after the initial point of saturation has been reached would appear to be of no value. For a severe "B_1" deficiency one week of large doses of the vitamin should be adequate. After this period the dosage can be considerably reduced.

A most careful experiment was conducted on a human being by Elsom, Lewy and Heublein.[46] The writers call attention to the variety of claims that have been made as to the value of the various factors of the B Complex in many clinical conditions. Many of these claims are based on uncontrolled observations and their validity is therefore difficult to assess; only when the environment has been carefully controlled and coexisting deficiencies eliminated can a reliable estimate be made of the rôle of vitamin B factors in clinical medicine. With this in mind, a healthy human volunteer, a woman aged 60, was studied for one year, in 1933. She consumed a diet deficient only in vitamin B Complex. An extension of the observations made at that time was made on the same individual, five years later. This repeated experiment was the same in all essentials, but it employed more detailed methods of study and noted the effects which were unknown in 1933. In brief, the clinical manifestations of "B" deficiency were studied in an otherwise healthy individual who consumed a constant daily amount of a standard diet, adequate in all respects except for the B Complex. These clinical manifestations responded somewhat to thiamin; and were influenced very little by the addition of riboflavin; but were relieved by the administration of brewers yeast. An increase in the pulse rate was caused by the deficiency; cardiovascular abnormali-

ties subsided when thiamin was given. Gastro-intestinal symptoms developed during the deficiency, and were associated with X-ray evidence of delayed motility in the small intestine. Neither the gastro-intestinal symptoms nor the delayed motility of the small intestine were relieved until brewers yeast was added to the diet. During the deficiency, the neurologic symptoms were mild and were accompanied by a decrease in the electric irritability; these abnormalities disappeared following the administration of thiamin. Mental symptoms were prominent; they responded somewhat to thiamin, but were not relieved entirely until brewers yeast was added to the diet. During the deficiency, a mild macrocytic anemia developed; this was uninfluenced by either thiamin or riboflavin — but was relieved after the woman had received a general diet and brewers yeast for four weeks. Edema of all extremities appeared early in the deficiency; and a gradual loss of body weight occurred. In spite of the presence of edema these conditions were uninfluenced by giving thiamin or riboflavin; but the edema disappeared and the body weight returned to normal only after the administration of brewers yeast. In the study of this woman, the writers compared the findings in 1933 with those in 1938. Certain similarities and certain differences were noted. In each instance the outstanding clinical manifestations were changes in body weight, fluid balance and signs referable to the cardiovascular, gastro-intestinal, neurologic and hematopoietic systems. In each instance, approximately five weeks elapsed before the signs of the deficiency were definite. In 1933, however, glossitis and neurologic abnormalities were prominent; in 1938, these were comparatively mild. In the present experiment, anemia, and mental and cardiovascular symptoms were more pronounced. While reasons for these findings are not clear, it is important to realize that no single sign or symptom can be relied upon to provide a diagnosis of a deficiency. The outstanding finding of this study is that, almost without exception, the response to the individual components of the B Complex was both temporary and incomplete; and a return to normal occurred only after the administration of brewers yeast.

Street, Cowgill and Zimmerman[47] state that dogs maintained on a diet consisting of the B vitamins — thiamin, ribo-

flavin and the filtrate factors — but not "B_6," developed severe anemia. Treatment with "B_6" led to a rapid increase of erythrocyte and hemoglobin levels — whereas treatment with iron sulphate produced no response. Degenerative changes were found in the myelin sheaths of the peripheral nerves and of the spinal cords. Control animals received the same diet, except that they received "B_6" also — and they did not become anemic.

Flexner and Chassin[48] studied urinary excretion of pyridoxine after an intravenous test dose of the vitamin, 98 times in 84 patients. Eighty-eight per cent of the patients under 50 years of age excreted in one hour an average of 8.4 per cent of the amount injected. Seventy-one per cent of those over 50 years of age showed an average output in one hour of 7.2 per cent. The remaining 29 per cent — or 13 individuals excreted on an average of 2.3 per cent. A test dose on the basis of body weight rather than age was found to be probably more accurate. Ten patients between 5 and 15 years of age excreted 21.3 per cent of the amount of pyridoxine injected. Six of seven patients suffering from postencephalitic Parkinsonism showed an average of 2.5 per cent output of pyridoxine with the test dose. Twelve of 14 patients with different degrees of renal insufficiency showed a definite decrease in the excretion of pyridoxine.

Spies, Stanberry, Williams, Jukes, and Babcock[49] state that in order to test the toxicity of pantothenic acid in human beings, varying amounts of calcium or sodium salts were administered intravenously to 15 people. No reaction and no significant change in blood pressure, pulse, temperature and respiration were observed when 100 mg. of either salt was injected. The blood and urine were assayed for pantothenic acid before and at intervals after injection. An increase of 50 per cent above the preinjection level was noted within the first three hours after injection, but returned to normal in 24 hours. The urine concentration was similarly affected. The content of riboflavin in the blood increased 80 per cent and the pantothenic acid content 45 per cent on a dose of 200 micrograms per kg. The blood concentration of 28 patients with pellagra, beriberi and riboflavin deficiencies was 23 per cent to 50 per cent below that of normal persons. Injection of calcium pantothenate temporarily increases the concentration

of riboflavin in the blood, even of persons exhibiting riboflavin deficiency symptoms. Pantothenic acid appears to be essential to human nutrition and its function is probably associated with that of riboflavin.

"C"

Kastlin[50] states that fruit juices and fresh fruits are the chief sources of "C." It is commonly believed that milk is a rich source of "C"; mother's milk is approximately five times richer in "C" than is cow's milk. There is a rapid loss in "C," due to processing and pasteurizing cow's milk. Any food, whether vegetable or fruit, is also low in "C" if it is old by the time it is consumed.

The studies of Lund and Crandon[51] are particularly concerned with the determination of "C" deficiency among patients of all types in the surgical wards and the differences in the surgical convalescence of patients. As previously shown by one of these authors, the "C" level in plasma drops markedly after operation; and yet the patients show no clinical signs of scurvy even though the plasma level reaches zero. The work reported here was done by the method of Pijoan and Klemperer, in determining the amount of ascorbic acid, and later by the method of Mindlin and Butler. It seemed advisable to carry out further experiments on the development of human scurvy in a normal person. Crandon went on a scurvy-producing diet on Oct. 19, 1939, and continued until May 7, 1940. His diet consisted of eggs, cheese, butter, chocolate and coffee supplemented by adequate doses of vitamins A, B Complex, D and E. Three months after the diet had begun, a $2\frac{1}{2}$ inch experimental wound was made through the deep fascia of the lumbar region. Eleven days later a biopsy was secured. No defect in the wound healing could be demonstrated. It was five months before the first sign of scurvy appeared, which in this instance was petechial hemorrhages about the hair follicles of the legs. Three weeks before this, hyperkeratotic papules developed on the buttocks. These simulated lesions associated with "A" deficiency. There was slight lassitude and a tendency to fatigue easily, in four or five months — marked fatigue in the sixth month. No ecchymoses or changes of the gums occurred. At six months a second incision was made on the other side of the back. It

was difficult to suture the fascia — a difficulty not present three months earlier. This wound seemed to be healing by first intention. The cutaneous sutures were removed on the sixth day and on the tenth day the wound was opened for biopsy. It was found that the tissues under the skin had not healed and that the wound contained a dry blood-clot. That afternoon one gram of ascorbic acid was given intravenously and repeated daily for the next 10 days. The wound healed promptly. In over 100 operations on patients, the "C" level was studied for blood plasma. Complications of atelectasis and pneumonia were studied in certain of these patients. They found no correlation between the "C" intake and plasma levels. A dietary history should be taken on all patients who come to major surgery and if "C" deficiency is suspected, the patient should receive one to four grams of ascorbic acid daily.

"C" and serum protein levels in wound disruption were studied by Hartzell, Winfield and Irvin[52] who collected a series of 1,458 of such cases. Undoubtedly many patients are operated on who are in a state that might be called "subscurvy" — and yet they have normal wound healing. However, in those who have poor wound healing we should determine the status of "C" and serum protein. Wound healing is affected by many factors, and the nutritional condition of a patient is a most important one. Either to maintain life or to repair tissue, there must be a supply of proteins, fats, carbohydrates, minerals, water and vitamins. Periods of inanition or faulty nutrition are likely to deplete the carbohydrates and fat stores and produce lower serum protein and vitamin levels. In a routine surgical experience, we must all universally supply carbohydrates and salts by intravenous administration; but, generally speaking, if a transfusion is given it is because the hemoglobin and the red blood cell count are low — rather than because of a low serum protein. As to the vitamins — usually they are forgotten entirely. It would seem logical that if normal healing is to be expected, the "C" and serum protein levels of the blood plasma ought to be brought to and kept at normal concentration.

Heinemann[53] recalls that diagnostic significance was first ascribed to capillary fragility in 1909, when it was found to be almost regularly associated with scarlet fever. In 1914,

its frequent occurrence among scorbutic children was first reported. Ultimately it was discovered that capillary fragility may be noted in a great variety of diseases. Capillary fragility is tested by applying to the upper arm a blood-pressure cuff, in which the pressure is maintained midway between the systolic and diastolic pressures for five minutes. The results are expressed by counting the number of petechiae in a measured skin area. Less than 10 per square inch are interpreted as within normal limits. This quantitative evaluation, however, creates an impression of accuracy not supported by statistical data. More reliable chemical methods are now available. The term "saturation" may be defined as the condition in which the "C" content of the body is at a theoretic optimum. In this state, further increments of "C" are rapidly eliminated through the kidneys. "C" deficiency, then, can be defined as the extent to which an individual falls short of this theoretic optimum. The degree of this deficiency is determined by saturation tests, which consist of the measurement of the urinary output of "C," during the administration of 4 mg. per kg. of body weight per day, until the 24-hour excretion exceeds 50 mg. This urinary surplus excretion of "C" does not occur unless saturation is attained, since the avidity for "C" in the tissues of a depleted organism is such that test doses of the aforementioned magnitude are completely retained. Case reports are presented which indicate that the capillary fragility did not correspond to the degree of "C" saturation or deficiency, nor was any decrease of capillary fragility noticed after saturation had been completed. Capillary fragility varies greatly even among healthy subjects. The capillary fragility test is certainly nonspecific; however it cannot be questioned that in certain instances capillary fragility, really and exclusively, is caused by lack of "C." In brief, capillary fragility can be identified as a manifestation of "C" depletion, only in retrospect. Except for purposes of special investigation, adherence to the capillary fragility test as a means of studying "C" deficiencies, seems no longer justified. The capillary fragility test continued to be used after and in spite of the introduction of clinical methods, chiefly for two reasons: *1.* Analysis of urine has been made without proper precautions and *2.* Analysis of blood plasma is often found to have little diagnostic value. Analysis of single specimens of urine gives entirely unreliable

information. Accurate information can be secured from the analysis of whole blood. The concentrations of "C" in whole blood have been shown to be directly correlated with the amounts of the vitamin required for saturation. For practical purposes the determination of "C" content in whole blood is the most satisfactory diagnostic procedure. Potatoes have been underrated as a source of "C." For the population of a large part of Europe, potatoes were and still are a more important source of "C" than citrus fruit — which has been notorious because of the compulsory diets of English sailors — from which their nickname "Limies" was derived almost 200 years ago. The introduction and large scale cultivation of potatoes in Europe stopped the severe epidemic of scurvy that had formerly prevailed. In Holland, the annual number of deaths from scurvy declined from 300 during 1875-1884 to about 50 for the period of 1895-1899. Stefansson, the explorer, showed that a man can be protected against scurvy by a source of "C" as poor as fresh meat; he and his expeditionary friends remained free from scurvy during several years in the Arctic, as long as they lived on fresh meat. When a few of his comrades found and consequently used canned foods (including meat) they promptly developed scurvy — which was cured after a fresh-meat diet had been reinstituted. Fresh meat contains about 2 mg. of "C" per 100 gms. The recommended dosage of "C" frequently exceeds the actual need. One pint of orange juice daily has been advocated for a child, with the claim that it prevents dental caries; such an amount, at least 250 mg., would safely protect an entire family. It has been suggested that in biologic effects, synthetic ascorbic acid and naturally occurring "C" are not identical. Whereas no definite conclusions are justified as yet, a preference is justified for oranges and other foods rather than ascorbic acid for regular dietary purposes. One orange yields from 60 to 100 cc. of juice, containing an average of 0.5 mg. of "C" per cc. Actually, an orange provides considerably more than that present in the juice because of the adherent traces of peel — which is especially rich in "C." Fifty mg. of "C" from oranges costs about four cents — and this is the price of one 50 mg. tablet of ascorbic acid. Oranges are superior to ascorbic acid in that they provide food value as well as "C" itself. Ascorbic acid, on the other hand, can be accurately measured as to dosage and can be administered paren-

terally; also much larger doses of "C" can be supplied as ascorbic acid than in the form of orange juice. The synthetic product is further indicated wherever fruit juices are not tolerated.

Murphy[54] studied "C" nutrition in 86 school children in a Maine village. Studies were made during the late fall of 1938 and the early spring of 1939, because "C" containing foods are less abundant at this time. Most of the children were of French Canadian extraction. Analyses of 76 of the fall dietary records and 63 of the spring records showed that only one child in seven had the minimal standard of one good "C" food daily. Particular attention was given to the storing of each food and the cooking of it. The "C" content of their potatoes decreased from 0.17 mg. per gm. in the fall to 0.11 per gm. in the spring, due to storage alone. The loss during cooking represented 27 to 55 per cent for potatoes, 46 to 67 per cent for cabbages, 14 to 50 per cent for rutabagas and 29 to 56 per cent for greens. 32 per cent and 51 per cent of the children showed oral manifestations of the deficiency. 58 per cent and 40 per cent of the dietaries examined were found to be markedly low in "C."

Rafsky and Newman[55] selected 25 individuals whose ages ranged from 56 to 83 years. Fourteen were men and eleven women. All of these individuals were in apparently good health. All of them received comparatively large doses of "C." Only two showed a more or less constant saturation point. In the others, high retention values were observed; in fact, in seven cases the amount of retained "C" continued to increase throughout the experiment.

Sweany, Clancy, Radford and Hunter[56] made an extensive study of "C" and its relation to tuberculosis. Studies on "C" saturation were made in 79 patients; and on treatment of the disease with "C" on 282 patients, of which 128 were studied for more than one year. Postmortem studies were made on 32 patients and their organs were analyzed for "C" content. In moderate or early advanced cases, the "C" content was slightly below saturation after 10 to 12 days on a basic diet of 31 mg. a day. In more advanced cases, exhaustion of "C" was proportional to the severity of the disease, and the intake of the vitamin. A patient with severe tuberculosis is capable

of diverting large quantities of "C" (up to 150 mg. a day). Patients on peptic ulcer diets, non-residue diets, alcoholics and surgical patients show a reduction of "C" below the saturation point. In certain cases it may be more suitable to supply "C" by intravenous injection in the form of a salt of ascorbic acid. There are roughly 5 mg. of "C" per 100 gm. of total body tissue, which represents a total of 3 to 5 gm. of "C" in the entire body. The concentration of "C" is highest in the glands of internal secretion — hypophysis, gonads, adrenals, pancreas and thyroid. A relatively high level of "C" is maintained in the liver and brain even when depletion is severe; in fact the liver and the brain contain three-fourths of the entire supply in the body. When tuberculosis is far advanced in patients, large doses of "C" are beneficial. No benefit was noted when "C" was given to a point in excess of saturation.

"D"

Rapaport[37] states that cod-liver oil contains six different compounds capable of "D" activity. Two of these compounds are more important than the others. "7-Dehydro Cholesterol" is responsible for the "D" activity of cod-liver oil and many other fish oils. This same substance is formed when milk is irradiated or when the skin is irradiated. It has been called "vitamin D of animal origin." "Activated Ergosterol" is formed by the irradiation of ergosterol by ultraviolet rays. It is the active ingredient of viosterol. Ergosterol is obtained from plants and has been called "The vitamin D of plant origin." "D" maintains the calcium and phosphorus concentrations of the body fluids at levels which promote calcification of bone. It does this by increasing the absorption of calcium and phosphorus from the intestinal tract. Recent evidence indicates that it also acts upon the renal tubules to regulate phosphate reabsorption. The adult bone is not inert or static; its calcium stores are constantly being withdrawn and replaced, and the normal adult bone is the result of equilibrium between these two processes. In the absence of "D," withdrawal of calcium continues — and osteomalacia results. "D" should be given throughout life, for there are almost no natural foodstuffs which provide adequate amounts of this substance in the quantities of food ordinarily taken in the

American dietary. It should be started in the third week of life, at a level of 800 units daily (two teaspoonfuls of cod-liver oil or five drops of concentrate). This is further increased, from 10 to 15 drops daily during the first two years of life. After this, one teaspoonful of cod-liver oil or two to three drops of concentrate suffice. These amounts are purely arbitrary, since the "D" requirements of childhood and adults have not been precisely determined. There are circumstances in which this vitamin should be given in larger amounts. Premature infants require more. Patients who are unable to obtain exposure to sunlight — invalids, factory workers and others — need "D" in larger amounts. When there is poor absorption of fat, water-soluble Drisdol or ultraviolet irradiation is to be recommended.

Andersson and Nylen[58] report the histologic findings in experimental hypervitaminosis D. Tobeck had previously described changes in the otic capsule following the administration of large doses of "Vegentol," and stated that the changes found resembled otosclerosis. The authors studied the temporal bones of white mice and also pregnant mice, who had received fish-liver oil and ergosterol. They observed no changes in the nerve, ganglia or sensory organs in the internal ears of these animals. There was degeneration and necrosis of some of the bony cells; and the intercellular substance appeared as fine granulations. Osteoporosis was observed in the temporal bones of the pregnant mice. Osteoclasts were present in medullary cavities and in the vascular channels of the bone. These alterations, however, showed no resemblance to the lesions typical of otosclerosis.

"E"

Ervin[59] states that during the past few years "E" deficiency has been shown to cause abnormality of the cross-striated musculature of the body and also to produce lesions in the central nervous system. Prior to this time "E" was considered to be of value in reproduction only. H. M. Evans has shown that wheat germ oil contains beta and alpha tocopherols. A lack of the alpha factor is concerned with muscular atrophy. "E" is resistant to heat, alkalis, and acids. There is no definite information as to the necessary requirements of "E" for man. Abortion in cattle, sheep and swine

may be corrected by "E." The larva of the honey-bee develops into a queen when it receives "E." A deficiency of "E" differs for the two sexes. In the male animal, histologic lesions make their appearance in the testes and seminal tubules. These may cause permanent sterility. The female animal deficient in "E" may have a litter but she refuses to raise them. It has been assumed on the basis of animal experimentation that habitual abortion in the human female is due to "E" deficiency. Clausen believes that the value of "E" for the treatment of menstrual disorders, failure of lactation, and vaginal pruritis is not definitely proven. He does not feel justified in crediting "E" as a definite aid in the treatment of habitual abortion. Widenbauer suggested that premature infants might suffer from a deficiency in "E" inherited from the mother. He treated 17 such infants with "E" and produced a rapid increase in weight in 11 of the 17 after a previous arrest of growth. Wheat germ oil is at the present time the best natural source of "E."

Studies by Steinberg[60] suggest that primary fibrositis may turn out to be a metabolic rather than an infectious process. Evans and Burr were the first investigators to describe a spastic paralysis occurring in the suckling young of rats — when the mothers were deprived of "E." At 21 days these sucklings began to show difficulty in getting on their legs when placed on their backs. The disease increases in severity during the ensuing four to five days and by the twenty-fifth day of life, practically all the animals destined to develop the disease may exhibit it. All attempts to cure the disease fail, after it has been established for several days. However, the disease is prevented if the mother's diet is shifted from an "E" deficiency diet to one rich in "E," on the day of birth of the rats. It is already too late to forestall disaster if the shift to an "E" rich diet is delayed until the earliest appearance of paralysis in any member of the litter. Experiments and experiences by several others caused the writer to try the clinical effect of "E" in the treatment of fibrositis. This condition may be defined as an inflammatory reaction of fibrous connective tissue present anywhere in the body. The pathologic picture found in fibrositis and that described by Pappenheimer as occurring in ducklings on an "E" deficient diet, are practically alike. Fibrositis may occur

as a primary disease or as a secondary disease. Internists are familiar with the muscle pain, swelling and pain associated with atrophic arthritis or gout. They have seen painful swollen bursae associated with many of the rheumatic diseases. Very few are familiar with the disease as a primary one. Many common diseases are in fact evidences of primary fibrositis but masquerade under various titles — such as lumbago, torticollis, muscular rheumatism, tendonitis, periarticular fibrositis, panniculitis, myositis, and so on. Wheat germ oil was given in doses ranging from 2 to 8 cc. to 82 patients; 30 with primary fibrositis, 20 with fibrositis secondary to atrophic arthritis, 20 with fibrositis secondary to hypertrophic arthritis, one with fibrositis secondary to gout, 3 with sciatica of unknown cause and 8 neurotic patients. All of these cases had been observed for a period of three months to two years, under different methods of therapy. The wheat germ oil was taken in equally divided doses three times daily. All of the 30 cases of primary fibrositis were relieved of all symptoms. Two of them had only mild relief after having received 3 cc. of wheat germ oil daily for four weeks. They then received a preparation of "E" — which contained 120 mg. of naturally occurring alpha tocopherol. After one week of such therapy they were completely relieved of all symptoms. Of the 20 cases of atrophic arthritis, 8 noticed improvement in muscle soreness and stiffness; 12 experienced no relief. Of the 20 cases of hypertrophic arthritis, none noticed improvement in the soft tissue structures. Similarly the case of gout had no relief from the extreme muscle soreness. No relief came to the 3 cases of sciatica, of unknown cause. In brief, it appears that "E" is of value in the treatment of primary fibrositis, but of little or no value in the treatment of secondary fibrositis.

"K"

The history and clinical use of "K" is discussed by Mehlman.[61] Henrik Dam of Copenhagen in 1928 placed chicks on a fat-free diet; and after a period of several weeks, observed fatal spontaneous hemorrhages from the wings, skin, and gastrointestinal mucosa. From this he suspected that some fat-soluble substance was necessary for the maintenance of

normal antihemorrhagic properties. He then discovered that there was a marked fall in the prothrombin levels of these chicks. This research was followed by an attempt to isolate and identify the substance. It was found that the administration of the nonsaponifiable, nonsterol fraction of hog-liver fat or of alfalfa, was effective in preventing the occurrence of this sort of hemorrhage — or of curing it after it had already made its appearance. This antihemorrhagic factor was named vitamin K, from the Danish "Koagulation." Ten years have elapsed since the existence of an antihemorrhagic vitamin was first suspected; recently it has not only been chemically identified, but synthesized. The coagulation theory of Howell has been fairly well accepted: The reaction occurs in two states; first, the prothrombin, calcium and thromboplastin interact to form thrombin; second, the thrombin thus formed acts on fibrinogen, to form fibrin. For detecting a "K" deficiency, the method of Quick has gained wide acceptance: Blood is drawn from a vein and oxalated. The plasma, obtained by the centrifuge, is mixed with an optimal quantity of thromboplastin — prepared from animal brain or lung tissue; and a measured amount of calcium chloride is then added to the mixture. The length of time required for clotting is measured as the "prothrombin-time." Normal values are from 18 to 24 seconds. It is found that hemorrhages do not occur unless the time is 40 seconds or longer — or the prothrombin level, calculated from the prothrombin time, drops below 20 per cent of normal. A rapid bedside method, useful for clinical purposes, was developed by Ziffren, Owen, Hoffman and Smith: Thromboplastin, freshly prepared from ox or rabbit lung (0.1 cc.), is placed in a test tube and whole blood is added (0.9 cc.). The tube is inverted and then tilted at one second intervals until clotting occurs. The time is measured with a stop-watch and is compared with the time required for clotting to occur in the blood of a normal individual. Although this method is admittedly rough, and measures not only the prothrombin activity but the summation of several other factors, it is sufficiently accurate for most clinical purposes and requires a minimum of materials and reagents. Hemophilia appears not to be a disease in which diminution in thromboplastin is the chief factor; the most promising work seems to suggest that the deficiency lies in an abnormal resistance of the platelet to lysis, due either to

an inherent change in the platelet or to a change in the blood serum. Within the past two years numerous reports have appeared as to the clinical value of "K." The chief indications have been of obstructive jaundice with tendency to bleeding, postoperative bleeding, and hemorrhagic disease of the newborn. It is well known that fats are absorbed from the gut after preliminary hydrolysis, saponification, and interaction with the bile salts normally present. In the absence of bile salts, fats are poorly absorbed and "K" then shares their fate. In most cases, the oral administration of "K" and bile salts will cause an almost dramatic return of prothrombin-time from levels of 60 or more seconds, to the normal value of about 20 seconds, within a period of 6 to 24 hours. Quick and Grossman studied the prothrombin-time in a series of newborn infants, and concluded that the prothrombin level at birth is nearly normal, but rapidly declines in the first few days of life, returning to and maintaining a normal level on about the fourth or fifth day of life. They believe that food intake during this time is too insignificant to account for the rise observed, and they attribute it to the onset of bacterial activity in the intestine, which begins shortly after birth — as soon as bacterial organisms enter the mouth with sucking. The onset of the condition is apparently due to inadequate storage of "K," and the condition is clearly due to a lack of this vitamin — because oral administration of "K" causes a rapid rise to the normal level. Certain problems still remain to be worked out: *1.* The daily human requirements of "K" for maintenance of normal prothrombin levels. *2.* The clinical dosage and the preferable routes of administration of the various synthetic "K" substances. *3.* The physiology and biochemistry of prothrombin, and the part that "K" plays in this process. *4.* An accurate method for estimating prothrombin concentration.

A survey of the work of others and a report of his original work on "K" is given by Andrus.[62] One of the most dramatic and stimulating series of events in recent years concerns the discovery of "K" — its isolation, the recognition of its rôle in the body, and its clinical application to the study and treatment of deficiencies. "K" is obtained from natural sources by extraction with fat solvents; and is found most richly distributed among the green, leafy plants and vegetables — such

as alfalfa, spinach, cabbage, cauliflower, kale, carrot-tops and seaweed. It is most abundant in the structures that contain chlorophyll, and is therefore to be found in higher concentrations in leaves, rather than in seeds, fruits or roots. Another rich source is putrified fish meal. Laboratory tests are available to detect the activity of prothrombin in the blood. The most accurate and consistent is a test by Warner, Brinkhous and Smith; this is more desirable for research purposes. However, the same investigators have more recently published a more simplified method which can be performed at the bedside or in the office — and this test gives results quite satisfactory for clinical purposes. Another method which is equally satisfactory for clinical work is that of Quick. The discovery of the existence of "K" and of its sources led to the production of more and more concentrated extracts until Dam and his co-workers, in 1939, reported a concentrate which they assayed as "20 million Dam units per gram." It was then recognized that while this extract and other extracts were very active, the "K" obtained from alfalfa was distinctly different from that from fish meal. The alfalfa extract was then termed "K_1" and that from fish meal "K_2." Another substance which had previously been isolated from the tubercle bacillus, was found to possess "K" activity. This is called "K_3." Again four groups of workers independently reported another compound that possessed "K" activity; this synthetic substance, now known as "K_4," is generally accepted as having the highest activity of all those so far studied. It seems to be even more potent than the crystalline vitamin compounds obtained from natural sources by extraction. These various forms of "K" are soluble in oil, but only slightly soluble in water. They can be given by mouth in either solvent, as well as intramuscularly. When given by mouth, bile salts are also administered — but these are of course not necessary when the vitamin is injected parenterally. The preference is for the injection in oil by the intramuscular route — as it is free from toxic symptoms and the effect of a single dose is maintained for a considerable period — as long as 11 days in one of the cases reported. As in the members of the B Complex, the numerical designation of the various compounds with "K" activity does not indicate any qualitative differences in their action. So far as is now known they differ only quantitatively. After absorption from the

intestine, "K" is stored in the body tissues. It is present in appreciable quantities in the feces of animals, even though they may be deficient in "K." Once "K" is absorbed, it is intimately concerned with the production of prothrombin. "K" must not only be absorbed from the intestine, but the liver must be normal in order to produce the optimal effect in maintaining the plasma prothrombin. There is remarkably little difference in the plasma prothrombin levels in normal individuals; even with relatively large doses of "K," it does not seem possible to elevate the plasma prothrombin activity above the normal level. For this reason there seems to be little danger that overdosage of "K" will produce thrombosis. "K" therapy is unavailing except in patients with conditions associated with diminished levels of the plasma prothrombin; it cannot be expected, therefore, to be of benefit in such diseases as hemophilia or thrombocytopenic purpura. The most striking type of K avitaminosis is seen in cases of obstructive jaundice. Due to absence of bile, the fat-soluble "K" is not absorbed — and seriously depressed plasma prothrombin levels result. Because the body normally has a fairly large reserve of "K," the fall is gradual and may not reach the hemorrhagic level for some time. When the prothrombin reaches the critical level — usually about 20 per cent of the normal — bleeding occurs.

Machella[63] states that "K" is formed in the intestine by the action of bacteria, and following absorption is converted by the liver into prothrombin. A prothrombin deficiency can be induced in chicks by means of a "K" deficient diet. In newborn infants a lower prothrombin level has been attributed by some to an inadequate amount of "K." Other factors may be the absence of bacteria or bile from the bowel, hypermotility of the intestine or an inadequate supply from the mother. In any event, hemorrhagic disease of the newborn can be controlled by "K." Faulty absorption of "K" from the intestinal tract may be caused by lack of bile salts from the intestine as in obstructive jaundice, bile fistula, or after prolonged duodenal aspiration, and many other conditions involving the gastrointestinal system. Oral "K" therapy under such conditions is usually disappointing. An intravenous or subcutaneous administration has to be resorted to. Methyl naphthoquinone may be administered intravenously, subcutaneously

or intramuscularly. If a patient with low prothrombin level does not respond to "K" therapy, and the cause is presumably due to hepatic damage, transfusions of fresh blood should be given. This will allow hepatic function to improve, and the utilization of "K" will be restored. Occasionally a patient with jaundice may have bleeding and at the same time a normal prothrombin level. This is probably the result of "C" deficiency or a low platelet count.

A case report of postoperative bleeding cured by "K" is presented by Chute.[64] A 21-year-old man who had always been healthy had had an uneventful tonsillectomy nine years before. He had never had any abnormal bleeding, nor was there any family history of bleeding. On the seventh day after an operation, the wound began to bleed, and for the next four days moderately profuse bleeding continued — both in the urine and from the wound. Prothrombin deficiency was demonstrated; and "K" was given by mouth. The next morning, the intrarenal and wound bleeding had decreased. "K" was continued. In operations in which the surgeon cannot ligate all the bleeding points, and must of necessity depend on the natural blood-clotting mechanism of the body, the prothrombin determination and "K" therapy may prove helpful.

A discussion of "K" and therapeutic experiences are given by Hauser.[65] The newer methods of prothrombin determination are based on the principle that the blood is first made uncoagulable and then a certain amount of thrombokinase solution is added. The author uses Hillman's milk as the source of thrombokinase. Three solutions are used. The prothrombin time is represented by the period from the mixing of the three solutions until a platinum loop moves through the mixture and gathers a "thread" from the mixture. With this method, the normal prothrombin time amounts to 20 to 60 seconds, usually 30 to 35 seconds. The author reports 10 cases under his own observation, with favorable results in obstructive jaundice, hemorrhages of the newborn, and in certain cases of sprue.

In a study of 30 patients with various diseases and prothrombin deficiency, Stewart[66] states that synthetic "K" may be taken orally or parenterally in doses of 1-4 mg. daily. No evidence of toxicity was noted after giving as much as 20 mg.

in one dose. The prothrombin response to treatment appears within 24 hours and lasts less than a week after the "K'" therapy is ended. In cases of severe liver damage and in chronic sepsis, the prothrombin deficiency may be refractory to treatment. The effectiveness of "K" taken by mouth is increased by taking bile salts, even in the absence of jaundice.

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VITAMINS AND THE EAR.*†

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Your Chairman recently suggested that I present a brief report of results of animal experiments and consider how the findings might be applied to clinical practice. To the clinician, and — far more important — to the patient, it seems most unfortunate that from the great mass of experimental work on the vitamins, so little practical information is as yet available. The basic information is vast, embracing as it does the work of investigators in almost every field of medicine and biology, as well as in veterinary medicine, agriculture and home economics. No doubt the future will reveal many practical applications of such studies, but at this time we cannot say that we have a positive approach to vitamin therapy.

GENERAL EFFECTS.

Before discussing the specific effects of vitamins on the ear we should certainly first consider their effects on the body as a whole — in development, growth and maintenance of health.

There is no doubt that proper nutrition of the body, particularly during periods of growth, is essential to both bony and soft tissues. During the critical period of development from the fetus to the mature adult individual, all food elements must be supplied in great abundance. Proteins, carbohydrates, fats and minerals are needed by the enlarging mass of tissues; and it is equally important that development be not retarded by the lack of an abundant supply of vitamins. A diet inadequate in any single vitamin during this period may be sufficient to retard growth and permanently impair the physical well-being of an individual for his entire future. Stature, muscular development, ability to cope with infections and establish immunity to disease, and the integrity of the nervous system are determined by many different

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†Contribution from the Department of Zoology, University of California, Los Angeles.

agents — including vitamins which are such a necessary and exceedingly important part of our diet.

As I. H. Jones[1] has expressed it, we have been limited to three methods of diagnosis: *1*. Diet, *2*. Laboratory tests, and *3*. Therapeutic tests. To them he has added the embryologic approach. Such an approach now enables us, by inspection of a lesion in the ear, the nose, or the throat, to select for therapeutic purposes a vitamin which is known to have a preponderant effect upon a tissue originating from one of the three germ layers. This embryologic approach is of particular value because of the limitations at the present time in the previous three methods. A study of the diet is not only laborious but by no means convincing, and at best leaves us with a rather vague concept. The laboratory tests that are as yet available are highly specialized; and in most communities throughout the country such tests are not even available. In certain instances, a therapeutic test can be made by oral administration, but in order to form a reasonably sure conclusion as to any vitamin deficiency one must look for a rather prompt response to its administration. This is best accomplished by injection; and six vitamins (thiamin chloride, riboflavin, nicotinic acidamide, pyridoxine, vitamin K, and ascorbic acid) can be so administered. The embryologic approach directs attention to a definite lesion and also to a definite structure. For the internal ear, a definite lesion is made apparent by means of vestibular and auditory tests. The value of the embryologic approach, regardless of the inaccessibility of the lesion, lies in our ability to interpret it in terms of one of the three germ layers. A particular vitamin therapy is thus indicated.

In our efforts to apply the results of animal experiments to humans we must be mindful of certain discrepancies. A three weeks old albino rat is placed on a deficient diet (lacking one single vitamin). During the first week manifestations of the deficiency become evident. These changes are marked or severe by the end of the third week. In human beings, this never occurs, because: Only one single vitamin has been omitted from the diet of the rat; it is not a mild deficiency of several related vitamins such as those of the B Complex for the human; and in addition, different animals show different responses to the lack of the same vitamin. Although fed on

a diet lacking in the same vitamin, the chick often shows signs and symptoms quite different from those in the rat. Neither nicotinic acid nor ascorbic acid deficiencies can be produced in the albino rat, because it actually manufactures each of these in its own intestinal tract. Consequently, caution is needed in interpreting experimental results in animals. At best, animal studies serve merely as clues to the clinician.

This difficulty might be overcome if groups of humans were to take various restricted diets for periods of time sufficient to show the effects of being deprived of a single vitamin. In a few instances, this method has already been applied with results of some direct significance.

VITAMIN THERAPY AND DISEASES OF THE EAR.

The results of the investigations to be presented are chiefly concerned with the histopathologic changes in the otic capsule, middle ear, internal ear and VIII Nerve.

THE OTIC CAPSULE.

The effects of experimental avitaminoses on the otic capsule are now well known (Mellanby,[2] Loch[3] and Covell[4]). Diets lacking or low in "A," "C," "D" or "E" produce lesions typical of each deficiency. Briefly, these are: *1.* Avitaminosis A. Increase in thickness of the periosteal layer sufficient to form circumscribed areas (exostoses) in the internal auditory meatus and modiolus. Mellanby considered that such overgrowth of bone caused pressure on the nerve with subsequent degenerative changes in it. *2.* Avitaminosis C. A replacement of the cellular marrow by that of the fibrous type in the periosteal layer characterizes this deficiency. *3.* Avitaminosis D. Characteristic bony lesions are to be found in the periosteal and enchondral layers. There is a replacement of rarefied bone by osteoid tissue. *4.* Avitaminosis E. This deficiency is associated with localized irregular thickenings of the periosteal layer.

The above changes in the bone are typical of each deficiency. Recently, Dr. A. F. Morgan, Department of Home Economics, University of California, reported on the relationship between vitamins A and D and the amounts of calcium and phosphorus in the diet. Indications of this relation-

ship were first evident in a series of rats. Later, dogs served as experimental animals for similar tests; and temporal bones of eight of these dogs were sectioned and stained for histologic study by the author. Two of the animals served as controls, one of which received normal amounts of vitamins A and D in the diet while the other one received excessive amounts of "A" and normal amounts of "D." There were no bony changes in either of these animals. A vertical section through the cochlea of the dog which received excessive amounts of "A" but a normal dosage of "D," is illustrated in Fig. 1. This is the control for the experiments. Two other dogs received normal amounts of "A" and high dosages of "D" (irradiated ergosterol). The bony changes in the capsule were similar in both animals. Fig. 2 illustrates the increase in bone of the periosteal layer, particularly in the vicinity of the cochlear nerve as it leaves the modiolus. Note also, in the basal turn of the scala tympani, a proliferation of fibroblasts and beginning new bone formation in the endosteal layer. Two other dogs received excessive amounts of both "A" and "D" in their diets. In this instance, the "D" was supplied in fish oil. There were no changes in the bone of the capsule in either of these animals. The remaining two animals received excessive doses of both "A" and "D" (irradiated ergosterol). One of these, probably because of its prematurity and runtiness, did not show the same changes as the other. There was excessive proliferation of the periosteal layer in the prematurely born animal with some evidence of resorption of bone, while the other one revealed no changes whatever.

These experiments suggest: *1.* Normal doses of "A" and "D" produce no bony changes; *2.* excessive doses of "A" and "D" produce no bony changes; *3.* normal dose of "A" and excessive "D" (either in the form of irradiated ergosterol or fish oil), result in proliferation of periosteal bone in the vicinity of the modiolus; *4.* these experiments show the importance of the proper prescribing of vitamin D, particularly to children, and the harmful effects of it when not *controlled* by adequate amounts of "A."

Mellanby[2] in 1938 reported the occurrence of bony hyperplasia in the otic capsules of dogs and other experimental animals lacking "A" in their diets. He examined 51 internal

ears from 44 dogs and studied serial sections of 16 of these from 12 animals. Litters of puppies (seven to ten weeks in age) received a diet consisting of separated milk, cereal (oatmeal, white flour, etc.), lean meat, yeast, peanut oil, irradiated ergosterol (vitamin D), orange or lemon juice, and sodium chloride. Therefore this diet consisted of ordinary foodstuffs, low in "A," plentiful in vitamins of the B Complex, and adequately supplied with "D" (irradiated ergosterol). In addition to this diet, control dogs received 30,000 I.U. of "A" daily. The dogs deficient in "A," over a period of four to

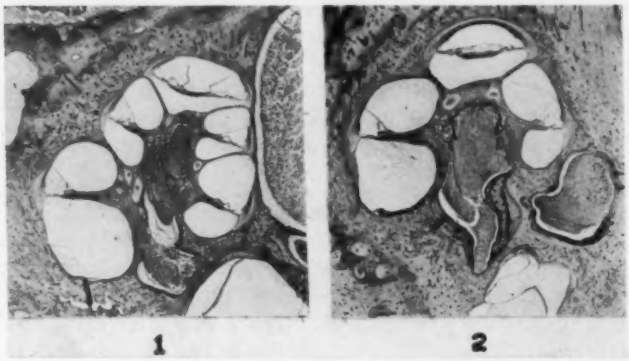

Fig. 1. Vertical section through the cochlea of a dog that received excessive amounts of "A" and also high dosages of "D" (irradiated ergosterol). There are no bony changes in evidence. Hematoxylin and eosin.

Fig. 2. Vertical section through the cochlea of a dog that received **normal amounts** of "A" and high dosages of "D" (irradiated ergosterol). There is considerable bony hyperplasia in the periosteal layer. A sizable exostosis encroaches upon the cochlear nerve within the modiolus. There is a tendency to new bone formation in the endosteal layer of the basal whorls of the cochlea. Hematoxylin and eosin.

10 months, revealed overgrowth of bone in the modiolus and also in the periosteal layer of the capsule near the brain; serous labyrinthitis with degeneration of the sensory epithelium in the ampullae and organ of Corti; and degeneration of cochlear nerve fibers and spiral ganglion cells with evidence of similar changes, to a lesser degree, in the vestibular nerve and cells of Scarpa's ganglion. The changes in the VIII Nerve and its ganglion cells, he attributed to the effects of bony hyperplasia within the modiolus by reason of the pressure and stretching of the nerve.

Changes identical to those described by Mellanby for low "A" were found in Morgan's experimental dogs which received normal amounts of "A" but excessive amounts of "D" in their diets. This caused the writer to come to the opinion that "D" should be controlled by adequate amounts of "A." Mellanby's dogs did not receive sufficient "A" in their foodstuffs. This illustrates how a diet low in "A" fails to check the action of normal amounts of "D." According to this concept, the changes in the bone were not caused directly by a diet low in "A" but were actually the result of "D." Therefore, when large amounts of "D" are given, large amounts of "A" should also be given.

THE MIDDLE AND THE INTERNAL EAR.

We will next consider the findings in the mucous membrane lining the middle ear cavity, the muscles controlling the chain of ossicles and the various specialized groups of the membranous cochlea.

Avitaminosis A: Experimental animals on a diet lacking in "A" show a relatively high incidence of middle ear infection. Here, as in other epithelial coverings, the lack of "A" produces keratinization of the most superficial cells and an accompanying cell metaplasia. Such a condition in the middle ear furnishes a fertile field for bacterial growth. Thus the changes in the epithelium due to "A" deficiency may be confused by a superimposed infection.

The effects on both cochlear and vestibular parts of the membranous internal ear are different. The specialized cells of the stria vascularis which secrete the endolymph, reveal degenerative changes, as do also the external sulcus cells and certain of the cellular groups represented in the organ of Corti. The cochlear nerve and the spiral ganglion cells are also found to be altered in animals maintained on a diet lacking in "A." The specialized epithelial cells of the vestibular end-organ show similar changes, although to a considerably less degree; the cells of Scarpa's ganglion and the vestibular nerve are less altered than the spiral ganglion and the cochlear portion of the VIII Nerve.

Avitaminoses of the B Complex: Considerable attention has been paid to the different factors represented in this

group, in order to determine the relative importance of each. In clinical practice, at the present time, the popular vitamins are "B_1" and nicotinic acid. The experimental results support the evidence that each of these is important but, in addition, other vitamins in the same group appear to be of equal importance. Middle ear infection, in animals, can occur with a lack of any one of the vitamins of the B Complex in the diet. However, none of the factors of the B Complex produce definite changes in the middle ear such as those found in "A" deficient animals. Some of the animals which were rendered deficient in "B_1," in "B_2," or in "B_6" then received the vitamin which each diet previously lacked — until they appeared normal again. Histologic examination of their middle ears revealed definite restoration of epithelium.

In order to evaluate the extent of damage to the external hair cells, external sulcus cells, spiral ganglion cells and myelin sheath of the cochlear nerve, a comparative study was made for each factor of the "B" group, except for nicotinic acid, pantothenic acid and the antigray hair factor. Most marked effects on the specialized epithelial cells of the membranous cochlea and on the nerve resulted in those animals whose diets had been deficient in "B_1," "B_2," or "B_6." Sectioned temporal bones of a nicotinic acid deficient dog showed changes in the cochlear nerve similar to those described for "B_1," "B_2" and "B_6." However, other material should be observed before degeneration of the cochlear nerve can be ascribed to nicotinic acid. The animals deficient in the antigray hair factor showed fewer changes in the VIII Nerve and internal ear than any of the other factors of the B Complex, with the exception of pantothenic acid deficient chicks. The filtrate factors for the animals studied would seem to be less essential to the membranous internal ear and nerves than other vitamins of the B Complex.

Avitaminosis C: A lack of vitamin C in the diets of young guinea pigs results in subperiosteal hemorrhages, fragility of the blood vessels, and painful and swollen joints. The middle ear cavity is filled with a serosanguineous fluid. The epithelial lining is not intact over all the surfaces of the cavity; and the submucosa is thickened because of hemorrhage and fibroblasts. The internal ear reveals some swelling of the cells comprising the organ of Corti — while only a slight change

is observed in the cochlear nerve fibers and the spiral ganglion cells. Changes to a similar degree are found in the epithelial cells of the ampullae, the nerve fibers of the vestibular part of the nerve, and the cells of Scarpa's ganglion.

Avitaminosis E: The fibers of the muscles of the middle ear are atrophic in vitamin E-low rats. However, low grade infection of the lining of the middle ear cavity may penetrate between the bundles of these two intrinsic muscles and result in degeneration of fibers, with atrophy and susequent fibrous tissue hypertrophy. Since many vitamin E-low rats are subject to infection of the middle ear, the muscle changes must not necessarily be ascribed to the diet. Suitable material for study of the membranous internal ear and VIII Nerve has not as yet been available.

COMMENT.

The following facts may be of assistance in clinical practice:

1. A diet complete in all vitamins is essential in the maintenance of and resistance to infection of the middle ear.

2. The development, growth, and maintenance of the otic capsule requires adequate amounts and proper proportions of vitamins A, C, D, and E.

3. The different parts of the internal ear, including the specialized sensory or hair cells of the organ of Corti have been shown to be altered, in vitamin deficient animals. The different vitamins of the B Complex are essential to the integrity of the epithelial structures of the cochlea and the vestibular portion of the internal ear.

4. Changes in the VIII Nerve and its ganglion cells (both cochlear and vestibular) result from deficiencies of the vitamin B Complex, and may occur in lesser degrees in other deficiencies. Periods of months and even years are necessary for the actual repair of nerve fibers; and for this reason no immediate recovery of the VIII Nerve can be accomplished by vitamin therapy.

5. It has been repeatedly emphasized in the vitamin literature that human deficiencies are of a multiple nature and treatment should not be restricted to a single vitamin.

6. The proof of the value of vitamins in the treatment of disease is an experimental problem which confronts the clinician. The whole concept of human dietary deficiencies will no doubt be revised as evidence accumulates.

SUMMARY.

With the exceptions of well-established vitamin deficiencies (beriberi, scurvy, pellagra, and rickets), as yet we cannot say there is a positive approach to vitamin therapy; and, at the moment, the actual prescribing of vitamins must be regarded as in an experimental stage. However, there is evidence, in most experimental animals, that a correlation exists between diseases of the internal and middle ears and a lack of vitamins in the diet.

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AMERICAN OTOLOGICAL SOCIETY.*

PRESIDENTIAL ADDRESS.

DR. GEORGE MORRISON COATES, Philadelphia.

In opening the scientific and executive proceedings of the Seventy-fourth Convention of the American Otological Society, the Presidential Address, as is customary, is the first item on the program. In fulfilling this obligation, let me say to you in all sincerity, that your President for the time being thoroughly appreciates the high honor you have bestowed upon him in selecting him as the leader of this oldest and most distinguished of national Otological Societies in the world. Merely as time goes, 74 years is not a long time, but in consideration of the wonderful otologic advances during this nearly three-quarters of a century, all preceding periods are dwarfed into insignificance. These 74 years constitute the era of modern otology, although it would seem quite evident that, in spite of all advances, only a beginning has been made of otologic contributions to human welfare. Many important problems remain to be solved, and with the accomplishment of their solution, other problems, now unthought of, will undoubtedly arise. The otologic millennium is still in the far distant future.

A resumé of unsolved problems is not contemplated in this brief address — it has already been given by one of the writer's distinguished predecessors in this chair. Brief comment will be undertaken on a few problems that have engaged the writer's interest during recent years without, however, any thought of aiding in their solution.

Perhaps the most spectacular and therefore to many, otologists and laity as well, the most interesting work before us today is the progress made towards the amelioration of progressive deafness by surgery. Two major approaches to this problem have been made. The first, consisting of the fixation

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of the secondary tympanic membrane by the placing of grafts in the round window, has been reported before this Society and, although not universally accepted or frequently practiced, has apparent possibilities, as shown by an increasing number of cases reported with improved hearing. The reported improvement in hearing comes on gradually and it is not known for how long a period the improvement will continue, but in no case has hearing been further impaired by this method. So far, very great improvement has not been claimed, so that in cases of from 50 to 60 dcb. loss in the critical frequencies, the hearing would still, even in most favorable cases, fall short of being useful. At present, it would seem, therefore, that the method should be employed only in cases where the deafness has not progressed to the point where a possible improvement of from 15 to 30 dcb. as the result of operation would raise the hearing level to a point of general usefulness.

Fenestration of the labyrinth in cases of otosclerosis and other forms of progressive deafness, where sound perception is still good, has been practiced sporadically for many years by experimentation in many countries. In properly selected cases, there can be no doubt of the *immediate*, spectacular improvement in hearing as the result of this procedure. This is in contrast to the slow improvement noted in the round window tissue graft operation, but the difficulty has been to prevent the fenestra from closing sooner or later by new bone formation or by fibrosis, in which case the gain in hearing is again lost, and sometimes more hearing in addition. It is a more dangerous operation than the preceding one, calling for consummate skill on the part of the operator, and has not been without bad accidents and even disastrous results. In the hands of American otologists the problem of keeping open the fenestra and therefore, in many instances, preserving the initial hearing increase, has been definitely more successful than heretofore, although just how this is being accomplished is not, at the present moment, surely known. This method has been proclaimed as a measure directed primarily for the relief of deafness due to otosclerosis, for which all other methods previously advocated have failed conspicuously. While this surgical procedure is being practiced by more and more otologists with variable, but, in most instances, with

some favorable results, it is very evidently not to be undertaken by the tyro but only by one well trained in the most meticulous technique of temporal bone surgery, and the danger is that it may fall into discredit by a failure to strictly observe this rule. It is an operation inevitably attended by grave danger, not only to remaining hearing but to the integrity of the vestibular apparatus, and even to life itself. Here again, it is contraindicated where decibel loss in the critical frequencies has progressed to the point where the expected improvement would still fall short of providing the patient with useful hearing.

With the great improvement in recent years of electrical hearing aids, the question arises whether many deafened patients would not do equally well by using one of these devices and so, with possibly a little inconvenience, avoid a serious operation, that at the best cannot guarantee success. While the time has not yet arrived where the otologist can, by the use of an audiometer, prescribe a hearing aid for the correction of his individual patient's deficiencies in various frequencies, yet by various combinations, by more or less of a trial and error method, and by many refinements in manufacture and design, a greatly improved result may be obtained. That this prescribing and fitting of hearing aids should be left in the hands of salesmen or inadequately trained fitters is no more desirable than that the prescription and fitting of glasses should be left wholly to the optician or the optometrist, yet this is the goal that many hearing device manufacturers seem to be striving for. The advantages of a thorough otological examination and survey would seem obvious, and the patient, after a fitting, should have his improvement of hearing, if any, checked by an otologist. Since this testing is for useful improvement of hearing and, therefore, intelligibility, some type of phonograph audiometer seems more appropriate than the standard pure tone machines.

The work of the various committees, both medical and lay, dealing with the prevention and amelioration of deafness, deserves more support than it is receiving. The deafened laity have been and continue to be active in this respect, and not only welcome but beg for otological support. May I ask the younger otologists, especially, to take an active part in the work of these lay organizations, the various Leagues for

the Hard-of-Hearing and of the American Association for the Hard-of-Hearing? The names of a few great men in our profession and specialty have been prominently connected with this work, Phillips, Hayden and Hays, of those who have passed on, and of the living, Berry, Newhart, Macfarlan, Sperry, Fowler, Hunt and a few others — but too few! It is through the efforts of these men and organizations that the national testing of school children has been undertaken and pushed to a partial completion, but so far much of this work has been confined to the detection of deafness — the attempted correction after discovery is still woefully behind. More state and local legislation is necessary to see that these handicapped children receive adequate care for the cure or arrest of the impairment, for continuing their education in special classes if necessary, for preferred position in the classroom, for hearing aids and for instruction in lip- or speech-reading. Here is a magnificent opportunity for service by our profession — if we do not rise to the challenge we will be subject to blame.

For a number of years past, otologists and dentists have been working on problems posed by morbid changes in the temporomandibular articulations caused by malocclusion or closed bite. Various causes are responsible for this condition, notably congenital malformations, irregularities of dentition, wearing away of the grinding, and therefore, supporting, surfaces of the molars, by the premature loss of these 12 teeth and by their replacement by physiologically ill-planned dentures. We are all familiar with the persistent work of Costen, who, by his careful studies, has demonstrated convincingly that certain types of neuralgias and head pains can be traced to this source. Not so familiar are the attempts to prove that certain types of deafness and tinnitus aurium have similar etiology, but the idea is growing that this may well be true, and if so, that otologists will have another weapon at their disposal in their war on impaired hearing. Persistent overbite, or malocclusion, caused by loss of support, especially on one side of the mouth, causes pathologic processes in these joints and in time leads to an irregular or swinging action of the jaws, with partial luxation of the condyle of the mandible. This condition is more common than is generally known. Since my attention was first directed towards this

region, I have superficially examined every hearing case coming to me, as well as many not complaining of impaired hearing, and in many of these I have noted evidence of a closed bite, the upper incisors coming well down over the lowers, the molars (either natural or artificial) not properly supporting the joints, a swinging motion of the chin and a noisy click or the feel of a partially luxating joint when palated with the fingers during wide opening and closing of the jaw. Not all cases, by any means, presenting this condition have neuralgia, deafness or tinnitus but a large enough proportion to be suggestive do.

Dentists have been conspicuous in the preliminary research in regard to this problem, but few practicing dentists have either enough knowledge or interest to be helpful in working out its practical application. Accurate Roentgenological studies are often helpful but here again few Roentgenologists, except those heading important services, are qualified to make or interpret such examinations. If such a condition is present and there is a reasonable suspicion that the patient's aural condition may be due, at least partly, to this factor, the obvious procedure would seem to be to open the bite by restoring normal occlusion. This cannot be done all at once because of pain and discomfort caused by the process and, in the hands of many dentists, it becomes a tedius, at times destructive and expensive operation, with, after all, uncertainty as to how beneficial the result will be. That trauma in the temporomandibular articulation could affect the external canals is easily conceived. It is not so easy to believe that the middle ear, the Eustachian tube and the inner ear can be so influenced. This subject was briefly presented by Dr. Wm. H. Crawford at the meeting of this Society presided over by Dr. Edmund P. Fowler. Munson, over 20 years ago, reported improved hearing by restoring the vertical dimension of the jaws by using artificial dentures. It has been recommended that worn-down molars be extracted and replaced by artificial ones for this purpose, which certainly seems radical. That certain changes do take place in the meniscus of the condyle joint as wearing down occurs is well proven, as well as pathologic processes in the tissues surrounding the head of the condyle and the glenoid fossa, as pointed out by Prentiss. Goodfriend has worked hard on the anatomic side of the

problem and has laid down definite normal measurements and angles, to which his prosthesis must conform. Much more work on this subject has been done which I am sure many otologists are not acquainted with. In most of it a simplified and practical application has been lacking. It is for this reason that I am glad to have on the program to be presented today a paper which presents these essentials, as well as an impartial estimate of the present situation of the fenestration operation, by observers who have had much personal experience with these two procedures.

At this time, as at our meeting in 1917, our thoughts are more or less occupied with the war news. For this reason, it seemed wise to present, in the nature of a symposium, a group of papers dealing with military subjects. May a merciful Providence prevent the necessity for putting into practice the important information that we will undoubtedly gain from these presentations! But if go to war we must, the Fellows of this honorable Society will be in the van wherever their services are most required. I trust we have not forgotten all the lessons learned in the last great war and that the younger members may benefit by our difficulties and mistakes. The group of papers, presented by eminent authorities, should bring us up to date.

I desire, in the name of the Society, to welcome the officers of the United States Navy who have so kindly consented to place their knowledge of special war problems at our disposal. It is also a pleasure to bid a hearty welcome to all our guests, members of our special branch of medicine or of any other, who may be present. And I wish to thank our most efficient Secretary, who was once our President, for his splendid work in arranging the programs for our Council meetings and in making the arrangements for this convention.

I now declare the Seventy-fourth Session of the American Otological Society open for the transaction of scientific and other business.

1721 Pine Street.

THE USE OF A TEMPORARY INEXPENSIVE BITE BLOCK TO DETERMINE THE RELATIONSHIP OF A CLOSED BITE AND TEMPORO-MANDIBULAR JOINT SYMPTOMS.*†

DR. FLETCHER WOODWARD, Charlottesville, Va.

During the past 20-odd years, it has been well established that a closed bite can produce dysfunction of the temporo-mandibular joint and cause symptoms in certain cases. But because of the variability of these symptoms and the expense and difficulty of establishing this relationship, many of us have hesitated to investigate and evaluate this syndrome.

Many articles have appeared in medical literature in regard to the mechanism, diagnosis, symptomatology and treatment of this condition. Notable among these are those of Dr. James B. Costen, of St. Louis. Likewise, many articles have appeared in dental literature by dentists and orthodontists. The problem is obviously difficult, and yet unsolved; however, it seems that enough facts have been established for us to seriously consider them.

In spite of this literature, I do not yet feel that we can attribute any certain symptoms to a closed bite, for we see many patients with a marked closed bite who have never experienced any discomfort. For this reason we have used a temporary, inexpensive bite block as a test in those patients whose symptoms are thought to be due to this condition before expensive prosthetic dentistry was advised. This serves to prove the relationship by relief of symptoms and also as a guide to the dentist in fashioning a permanent denture, should it be necessary.

Closed bite exists most often in those patients who have lost some of their molar, or molar and premolar teeth, on one or both sides, upper or lower, or both. If the dentist would replace all teeth following extraction, much future discomfort

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†From the Department of Otolaryngology, University of Virginia, School of Medicine.

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to his patients would be avoided. Closed bite can also exist when all teeth are present, if they have become badly worn, also when poorly made or badly worn dentures are present.

The physician is not alone in his confusion in regard to this problem, for many dentists seem to have very little information on either the symptomatology or the procedure to be followed in establishing a diagnosis, or the objectives

Fig. 1. Lips separated while jaws are held in relaxed position. Measuring wedge inserted, amount of separation, and teeth from which measurement is made is noted.

to be obtained in fitting a permanent denture. For this reason I would suggest that you work with some young dentist in your community, after first going over the literature with him and enlisting his enthusiasm and co-operation, for his knowledge, skill and equipment is necessary to carry out the diagnosis and treatment.

I will make no attempt to discuss the many symptoms that have been attributed to this condition, but will refer you to

the articles listed at the end of this paper. I would also like to say that we have not used X-rays of the mandibular joint for diagnostic purposes, because of the additional expense

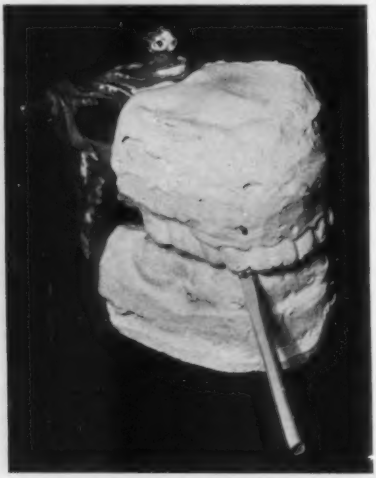

Fig. 2. Articulated model is locked after same degree of opening is ascertained, using same angle and same teeth as in Fig. 1.

Fig. 3. Articulated model with bite block in position.

and lack of precise information obtained, but have merely relied on the use of the test bite block which can be made at a cost of from $10 to $25 and will prove or disprove the relationship before expensive prosthetic dentistry or orthodontic treatment is employed. It also serves as an exact guide in the fashioning of these appliances or the ends to be obtained by orthodontic treatment.

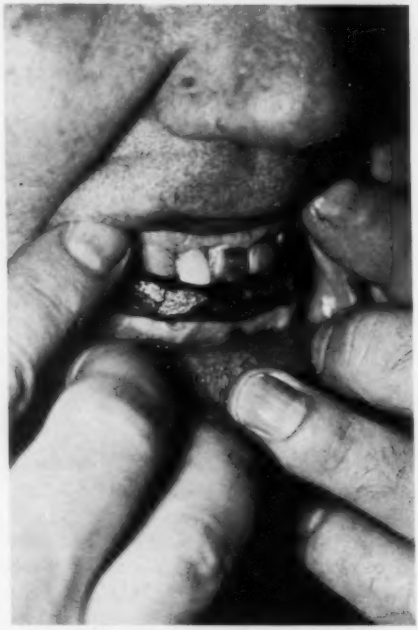

Fig. 4. Patient's mouth with bite block in position, over lower teeth.

The following description of the procedure has been outlined by Dr. David Massie, of the University of Virginia Hospital, and will be subsequently published by him separately in *The Dental Digest*.

The patient is first asked to completely relax the muscles of the jaw and face and allow the jaw to assume a position in which no effort is made to either close or open the mouth; at the same time observe that the lips are not rolled or

stretched in the effort to obtain this position of rest. The establishment of this position is most important and many times is quite difficult to obtain.

When this position has been ascertained, open the lips with your fingers and insert a tapering instrument or wedge between the premolar teeth, and note the exact amount of the opening and the teeth from which this measurement was obtained.

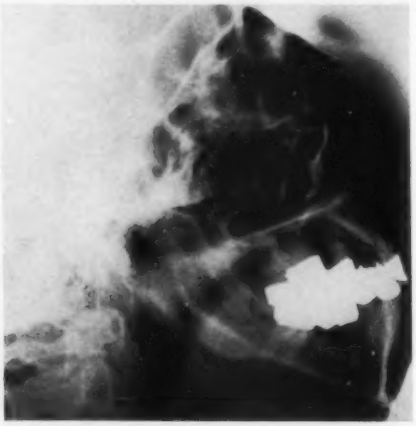

Fig. 5. Lateral Roentgenogram showed closed bite before introduction of bite block.

A modeling compound impression of the upper and lower jaws is next made so that plaster casts can be formed from them and mounted on an ordinary dental articulator.

The wedge is then inserted between the same teeth and the articulator opened to the previously measured distance and locked in this position.

A splint or hood of vulcanite rubber or shellac base is then molded over the lower teeth and edentulous spaces until the upper teeth rest comfortably on its surface in the articulated model. All rough edges are polished, and the bite block is complete.

The patient is instructed to wear this block for several days, except when eating, and then return for examination.

If it interferes with speech, it may need to be ground down a little; or if symptoms are not improved, it may need to be built up a little. In either case, after one is satisfied that the proper bite has been established, relief will either be obtained in two or three days, or we will know that the symptoms were not due to a closed bite.

When dental plates are worn, the position of the jaws is obtained and measured in the same manner; only in this case, heated dental compound is applied underneath the plate, as one would in making an impression for a rebase, until the desired amount of opening is secured.

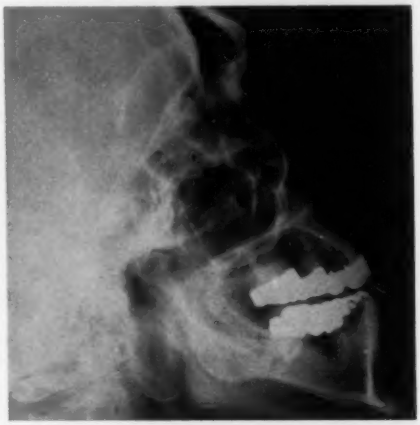

Fig. 6. Lateral Roentgenogram showing amount of separation of teeth after bite block is inserted. Bite block does not show on film.

When relief of symptoms is obtained through this procedure, the bite block is used as a guide in making the permanent denture; and since this is a matter of considerable expense, the assurance that relief will be obtained is a comfort to all concerned.

Many of these cases, especially those with a full complement of teeth, may need orthodontic care in order to obtain a permanent result.

Conclusions: A simple, inexpensive bite block is described and illustrated which will readily prove or disprove the rela-

tionship between a closed bite and the symptoms referable to the mandibular joint.

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VON RECKLINGHAUSEN'S DISEASE IN OTOLOGY.*

DR. CLARENCE H. SMITH, New York.

Von Recklinghausen's disease was the diagnosis of the pathologist on a recent biopsy. At the time, this name meant little to me and I was led to study the subject. I found it has importance in the etiology of acoustic tumors, and its manifestations may simulate other otologic entities. These facts prompt me to submit a resumé of this interesting disease.

Von Recklinghausen's disease is comparatively rare. In this disease, one observes the absence of any known etiological factor, the different clinical types and the lack of any beneficial treatment. It appears about once in 2,000 cases passing through the dermatological clinics. There is a Mendelian hereditary tendency which passes it on so that it recurs without a break in generations. The particular variety of clinical manifestations also seem to be governed by heredity.

It is thought that this disease is due to an embryological derangement, particularly of the ectoderm. There must be some mesoblastic involvement also to account for the changes in the bony structure. Some authorities think that an endocrine dyscrasia is responsible. The adrenals, pituitary and thyroid glands have all been considered causative.

Most cases show characteristic pigmentary changes and patches of a *cafe au lait* color. These changes appear at birth or early in life. The lesions are often numerous over the trunk; the face and extremities are sometimes spared. The pigmentation may be the only sign of the disease in some patients. When this is so, it has been called the incomplete form or forme fruste.

Skin tumors constitute the most common and most distinctive lesion of the disease. They vary in size and in number. They range from pin point size to that of an orange. They are usually soft, but may become hard and fibrous. They may be sessile or pedunculated. On section one finds a whitish

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gray tumor made up of masses of elongated cells, with oval nuclei arranged in parallel longitudinal rows. These tumors are massed at times and produce a diffuse swelling. One may find beadlike subcutaneous fibrous tumors along the course of the peripheral nerves, such as the median or the ulnar. The spinal or the cranial nerves may be involved. The acoustic tumors are similar histologically to the cutaneous neurofibromata.

Sharpe and Young[1] describe a condition they call elephantiasis neuromatosa. This consists of a diffuse overgrowth of the skin and subcutaneous tissue of the head, neck, trunk or extremities. More than one-third originate in the temporal region. It is generally unilateral. This condition appeared in the case I am reporting.

Pregnancy stimulates the increase in number of these tumors and also the size of the growth. Puberty has a similar influence.

The tumors are usually benign, but in some families there is a tendency for them to undergo sarcomatous changes. It is estimated that 12 per cent become sarcomatous. There is a tendency to recurrence after surgical removal and malignant metaplasia is common. These patients are poor surgical risks; they are very susceptible to shock and to profuse hemorrhage.

Radiotherapy is not advised as the lesions are extremely radioresistant.

Osseous changes are common. Scoliosis, abnormalities of growth, such as elephantiasis, subperiosteal cysts, osteoporosis and decalcification of the pelvis, cystic changes in the skull, thinning of the cranial vault, cerebral meningoceles are often seen.

Imbecility and other mental defects have been observed in some of these patients. It is estimated that the ratio of feeblemindedness in them is 20 times that of the population at large.

Margaret C., age 27 years, was seen in December, 1940. She was treated for a right-sided acute purulent otitis media. In the left temporal region there was a diffuse overgrowth of the skin and subcutaneous tissue. There was a slight amount

of discharge from the ear. The pinna had drooped and the external canal had collapsed. The drum was seen with difficulty (see Fig. 1, showing patient before operation).

The report of the X-ray examination was as follows:

"*Left Mastoid:* Above and behind the mastoid process is seen a large, irregularly round area of bone absorption. This

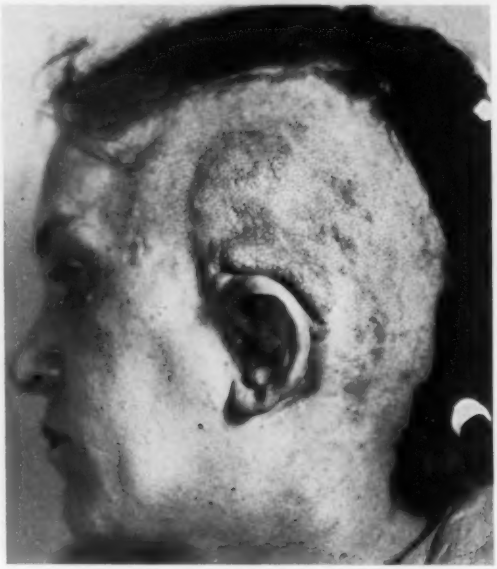

Fig. 1.

area extends down to the level of the upper part of the mastoid process. Within the area of absorption are seen several small islands of comparatively normal bone. The mastoid process itself shows normal structure of similar type to that observed on the other side. No definite evidence of inflammatory exudate is observed in the mastoid cells.

"*Conclusions:* The lesion is a bone destructive one; showing no evidence of bone regeneration. No evidence of inflammatory exudate is observed. From these findings, the logical conclusion is a neoplasm; probably malignant in character.

The possibility of cholesteatoma is the second alternative diagnosis." (See Fig. 2, showing X-ray picture.)

The patient said that the swelling in the temporal region had first appeared seven years before, and that it became larger after the birth of her first child. She said it was painless, and did not want to have it treated.

The process on the right side went on to an operative mastoiditis, and on Jan. 6, 1941, she was operated on for this.

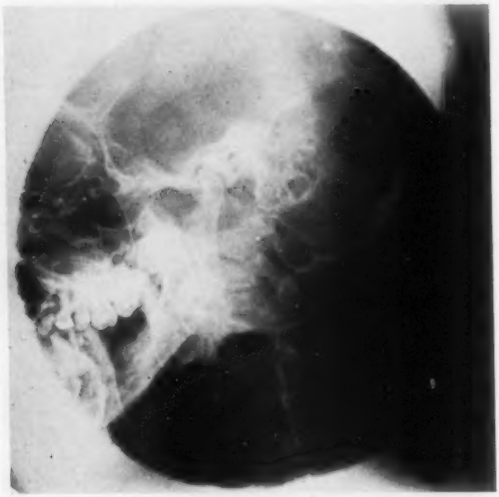

Fig. 2.

At that time she consented to have her left temporal and mastoid regions explored.

A Whiting incision was used to expose the left postauricular and occipital regions. When the bone was exposed posteriorly, a meningocele was found in the occipital region, about the size of a silver dollar.

In the postauricular and temporal regions, a collection of small tumors was found. A couple of these were removed for biopsy. The mastoid process was found to be infantile in type and it was normal in structure.

The report of the pathologist on the biopsy is as follows:

"*Gross:* Received two large and several small portions of reddish-yellow tissue. The larger portions each measure 2 cm. in size. On section they are yellowish, hemorrhagic and lobulated. The smaller portions are bone curettings.

"*Microscopic:* Sections contain a growth of circumscribed masses of fibrous tissue cells. Many of these are spindled with long processes; others edematous. Within these areas

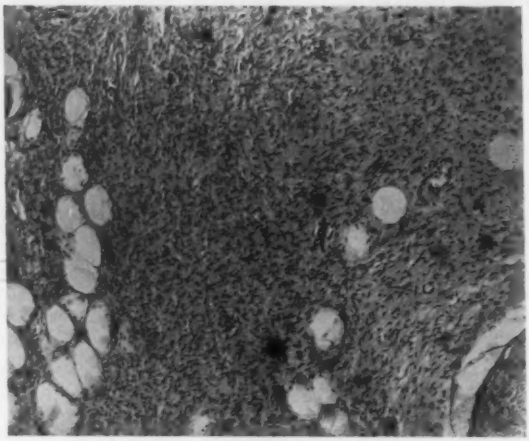

Fig. 3.

are bundles of spindled cells arranged in the typical 'palisading' seen in neuromas.

"*Diagnosis:* Neurofibroma of postauricular region. This is a benign tumor called 'Von Recklinghausen's disease'." (See Fig. 3, showing specimen.)

When the patient was examined more closely, it was found that she has numerous *cafe au lait* patches on her body, and there is a beadlike chain of small tumors along the course of the right radial nerve.

Her child, age 4 years, has a large *cafe au lait* patch on the anterior surface of the right leg.

Her baby, age 2 years, shows a pigmented patch on his back.

The patient's mother has pigmented patches on her shoulders, and she has a pendulous, soft, flabby tumor at the lower end of her spine.

COMMENT.

This is the report of a case of Von Recklinghausen's disease, with typical pigmentary changes, subcutaneous fibrous tumors along the course of a nerve, a large collection of typical neuronomata in the temporal region, and a meningocele.

There was distinct evidence of heredity, with direct transmission through three generations.

This case was of interest otologically because of the resemblance to a new growth in the mastoid region, with destruction of bone.

There are numerous reports of neuronomata attached to both auditory nerves in Von Recklinghausen's disease. Histologically, the tumors are alike, whether solitary, as in the ordinary acoustic neuronoma, or multiple, as in Von Recklinghausen's disease. Harvey Cushing,[2] in his monograph entitled, "Tumors of the Nervus Acusticus," stressed various points which are valuable in diagnosing this condition.

The auditory neuronomata comprise 6 per cent of all cranial tumors. They have a characteristic chronology of symptoms which is instructive. Otorrhea may be an etiological factor. It is thought that they may spring from a persistence and proliferation of the binding embryonal tissue in the acoustic fibres. Heredity plays no part in the solitary auditory neuronoma, and it is not to be considered as a manifestation of Von Recklinghausen's disease. They are commonest in the fifth decade of life. Patients with neuronomata generally are admitted to hospital after about four years' prodromal symptoms. The first symptom is tinnitus; this includes ringing noises, buzzing or roaring. Impaired hearing, gradually becoming worse, accompanies this. The deafness is rarely absolute. The vestibular branch is more often completely ablated than is the auditory branch. A degree of hearing may be regained after operation on the tumor. The vestibular

branch sometimes is affected before the auditory, and this accounts for a frequent mistake in confusing this condition with Ménière's disease.

The continuous pressure of the slow-growing benign tumor gradually dilates the internal auditory meatus, and this enlargement may be shown by Roentgenogram.

Unsteady gait and dizziness follow quickly. These symptoms may be from the involved vestibular nerve or from the centres in the cerebellum.

Discomfort in the suboccipital region is next noticed. Paroxysmal pain is felt sometimes in the frontal region, sometimes in the occiptal, sometimes radiating from back to front, with boring, retro-orbital pain. There may be soreness and stiffness in the neck. These symptoms are worse at night. They are probably caused by pressure against the tentorium, and irritation of the Vth nerve.

As the growth enlarges, extreme tenderness of the occipital muscles is complained of, and there is a protective tilting of the head, with the mastoid process leaning toward the shoulder.

As the disease progresses, cerebellar symptoms become more manifest, because of pressure against the flocculus and distortion of the cerebellar hemispheres and peduncles. Gait becomes more unsteady. The lower extremity is more apt to be inco-ordinate than the upper. There is a tendency to fall to the side of the lesion. Nystagmus from involvement of the cerebellum may be seen.

The adjacent cerebral nerves may next be affected from compression or distortion. The IIIrd nerve may be kinked or it may be constricted by blood vessels.

From involvement of the Vth nerve there may be slight paresthesia all over the territory supplied by the nerve. This shows itself in numbness, tingling and burning sensations. A valuable sign from the involved Vth nerve is the loss of the corneal reflex. This is, excepting the involvement of the VIIIth nerve, the most common evidence the cerebral nerves afford us.

Paralysis of the motor division of the Vth may paralyze the muscles of mastication and deviate the jaw toward the affected side.

Involvement of the VIth nerve caused double vision in two-thirds of Cushing's cases. This was probably caused by strangulation of the nerve by overlying vessels.

The VIIth nerve was involved in 19 out of 30 of his cases. This showed itself generally in a mild asymmetry in the lower face.

The glossopharyngeal, the vagus and the spinal accessory nerves make their exit from the cranium through the foramen lacerum posterior, and the hypoglossal nerve through its own canal, close to the internal auditory meatus. They show signs of pressure late in the disease, as evidenced by dysarthria and dysphagia, and paralysis of a vocal cord. Paralysis of the spinal accessory nerve might cause twitching of the trapezius muscle. In hypoglossal paralysis there is seen a deviation of the tongue towards the side of the lesion.

The general pressure symptoms are headache, nausea and vomiting, blurring of vision from choked discs, and a blunted sense of smell.

PATHOLOGY OF ACOUSTIC TUMORS.

They spring from the endoneurium peculiar to this nerve. The VIIIth nerve is engulfed by the tumor. Adjoining structures in the cerebellopontine angle are secondarily compressed. A pressure cone at the foramen magnum is one of the distant effects. Absorption of the inner lining of the skull from pressure may be present.

HISTOLOGY OF ACOUSTIC TUMORS.

There are two main types of tissue: dense, interlacing fibrous bands, and loose reticular tissue. The fibrous bands are made of masses of elongated cells with oval nuclei. The cells array themselves in parallel rows or whorls. In the loose reticular tissue are found fibrils in which fat and hyaline metamorphosis commonly occur.

These are the specific acoustic tumors, and are not to be confused with other growths arising in the cerebellopontine angle.

When these tumors are bilateral, as they sometimes are, they are a local expression of a more widespread process of the Von Recklinghausen type.

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140 East Fifty-fourth Street.

OTOSCLEROSIS WITH UNUSUAL PATHOLOGICAL FINDINGS.*

DR. MARVIN FISHER JONES, New York.

Otosclerosis causes impairment of hearing by other means than fixation of the stapes. Otosclerosis also causes other symptoms. Dizziness and facial paralysis are the two most notable.

Since the characteristic pathology occurring in the temporal bone was first called otosclerosis, the more unusual locations of this lesion have been reported by various investigators.

When the footplate of the stapes is ankylosed, the typical symptoms of impaired hearing, increased bone conduction, negative Rinne, paracusis Willisii, low tone loss with a retention of the ability to hear high tones have served to establish a clinical diagnosis of otosclerosis. Some authorities add to this list the necessity of obtaining a history of deafness in some blood relative. Tinnitus is a common symptom but it is not essential in making a diagnosis. In order to have a concrete conception in this presentation, the clinical symptoms I have named will be considered as diagnostic of otosclerosis with stapes fixation.

The fact that many errors are made in the clinical diagnosis has been proved by necropsy. The fact that many otosclerotic processes are discovered at necropsy which have failed to cause impairment of hearing is also accepted.

The number of cases meeting the symptomatic requirements outlined above is small. Because of the large number of cases reported as otosclerosis and because from this number many are now being advised to have an operation performed for restoration of hearing, and because there are patients who have otosclerosis causing nerve degeneration, it seems highly desirable for the purpose of statistical accuracy that some set of symptoms be given official recognition.

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This case with histological specimen presented will show some of the unusual symptomatic possibilities which have received mention in literature. I believe these more unusual phases should be emphasized.

The most common site of an otosclerosis is in the region of the oval window. The footplate of the stapes is frequently ankylosed. The first turn of the cochlea is another less common location and when the pathology is found in this region it may involve the promontory, causing exostoses into the labyrinth or extending into the middle ear cavity. A further extension may involve the bony spiral lamina of the cochlea (lamina spiralis), which involvement can and does cause a degeneration of the spiral ganglion, peripheral neuron of the acoustic nerve and Corti's organ. Corti's organ may also be destroyed by direct involvement. Otosclerosis may also involve the area of the round window. The degree of involvement may range from a slight encroachment to a total obliteration of the round window and its "niche." The last-named process may occur without involvement of the stapes.

Should the process extend into the modiolus, as it sometimes does, the whole acoustic nerve or any part may be destroyed. The clinical effect would probably be the same as that caused by the capsular involvement of the whole or a part of the cochlea.

The semicircular canals and vestibule may also be disturbed by otosclerosis. Otosclerosis located in these regions does cause dizziness and a disturbance in equilibrium. Either the cristae of the semicircular canals, the macular of the utricle and saccule or their nerves of supply and ganglion may be damaged.

The Fallopian canal housing the facial nerve is probably involved through an actural extension of the lesion from capsular bone. While the noncapsular bone is supposed to be free from otosclerosis, the expanding ability of the otosclerotic process may invade noncapsular bone to any degree. A facial paralysis caused in this manner would be by the pressure of an expanding mass rather than by continuity of tissue.

Cases have been presented which corroborate the statements regarding the location of pathology and the accompa-

nying symptoms. In 1899, Siebenmann reported a case and presented sections from the temporal bone showing foci in the semicircular canals. The patient complained of vertigo during the last few years of life (p. 48, Otosclerosis). In this case the canal of the facial nerve and the utricle nerve were also involved.

In 1900, Botey (p. 56) reported reduction of the size of the vestibule and distortion of the ampulae of the semicircular canals. No clinical history was obtained on this case.

In 1901, Haberman (p. 58) reported: "The round window was completely shut off by new bone formation from the tympanic cavity, except a narrow space filled with loose, meshed connective tissue containing a few fat cells, in front of the posterior portion of the membrane." Haberman also reported, in 1903, a lesion located "at the anterior periphery of the internal auditory meatus" and a projection into the labyrinth in the form of an exostosis. The later lesion caused an atrophy of the acoustic nerve plus Corti's organ.

In 1908, Bruhl (p. 74) also reported an involvement of the internal auditory meatus involving the basal convolution of the cochlea with resultant atrophy of the spiral ganglion and associated nerve fibres. He refers to a similar case previously reported by Sibenmann.

Grey made the following statement in 1906 (p. 81): "The cavity of the labyrinth is sometimes encroached on; and occasionally the round window is very much diminished in area."

In 1909, Manasse (p. 92) presented 19 specimens. These showed "a focus at the round window, a cone-shaped focus at the porus acousticus internus, its apex projecting free into the lumen, extensive resultant degenerative process in the nervous apparatus, especially at the spiral ganglion and Corti's organ." He also states that, "In only three of the nine cases did the disease extend to the stapes leading to stapes anklyosis. The latter is, therefore, not to be regarded as the essential feature of the disease."

In 1911, Mayer (p. 99) presented the report of a patient with otosclerosis, who had suffered from "vertigo and tinnitus." There had been a nerve degeneration in those branches supplying the equilibratory apparatus. He states,

"labyrinth atrophy, which can be included in the typical picture of otosclerosis."

Mayer states again the same year (p. 103) that three separate foci could be determined. One, an upper inner focus derived from the roof of the internal auditory meatus and occupying the cochlea from above down to about the middle of the cochlear whorl. Two, an upper outer focus surrounding the apex of the cochlea, continuous with the musculotubal canal and the facial canal. Three, a lower focus derived from the floor of the internal auditory meatus and surrounding the cochlea from below. Degeneration of Corti's organ is again mentioned by Mayer in 1913 (p. 103). Panse also mentioned the resultant changes in Corti's organ in 1911 (p. 105).

Alexander (p. 119) in his textbook, "Diseases of the Ear in Children," summarizes previous opinions to the effect that these pathological foci cause thickening of the lateral labyrinthine wall, a narrowing and ultimate osseous obliteration of the niches of the window, as well as stapes ankylosis. In certain cases bone foci protrude tumorlike into the labyrinthine spaces (vestibular cistern, scala tympani), more rarely are they found in the region of the semicircular canals in the region of the cochlea of the internal auditory meatus.

Frasier adds a specimen in 1918 (p. 125) which shows an encroachment on the vestibule. These findings have been observed, in whole or in part, by Wolf in 1914 (p. 130); Grey, 1915 (p. 141); Wittmaack, 1919 (p. 160).

Grey summarizes as follows: the localization of the pathological process is varied; almost any portion of the labyrinthine capsule may be affected; the margins of either or both windows, the walls of the cochlea, the apex of the cochlea alone, the semicircular canals or the walls of the porus acousticus internus. One more statement of Grey's seems most important: "Otosclerosis must not be regarded as a disease of the stapediovestibular joint."

Ruttin reports a complete obliteration of the facial canal in 1922 (p. 2140). In his report he states: "The otosclerotic focus came very close to the area cribrosa superior on the one side . . ." This close approach might readily account for the attacks of vertigo in otosclerosis.

CONCLUSIONS.

1. An official definition of clinical otosclerosis causing impaired hearing is desirable.

2. Impaired hearing with fixation of the stapes is not synonymous with otosclerosis. The symptom, impaired hearing, is part of a symptom complex having a much more comprehensive scope.

3. The concept of a fistulization of the semicircular canals for improvement of hearing in otosclerosis is misleading. Otosclerosis can cause degeneration of the acoustic nerve and Corti's organ. These patients may not be improved.

4. Vertigo, facial paralysis and loss of acoustic or vestibular nerve function may also be caused by otosclerosis.

121 East 60th Street.

ATYPICAL FACIAL NEURALGIA.*

DR. GEORGE H. HYSLOP, New York.

Lay people and physicians are careless in the use of the word "headache." They are also apt to be careless in their thinking about the symptom "pain in the face."

Patients are prone to tell about the part of the body which is the most conspicuous offender. If a patient's pain is predominantly in the face, he is apt to speak as though this was his only complaint. Questioning by the physician will determine whether a pain in the face is only one of a series of related symptoms. A correct diagnosis depends primarily upon a reliable and complete description of all the symptoms which are actually present.

The term "atypical facial neuralgia" applies to a group of symptoms which include pain outside of the trigeminal area. Frequently patients with such pain have vasomotor and secretory symptoms pointing to definite disturbance of function of the sympathetic. Sluder described a particular subvariety of this syndrome which has also been designated as "sphenopalatine" neuralgia.

Disease of the teeth, tonsils and sinuses may produce pain which simulates that of what is called "atypical facial neuralgia."

First, I will describe briefly a number of patients suffering from what I think can be called "atypical facial neuralgia." In listening to the clinical descriptions, your orientation may be clearer if I preface what I have to say by stating that I believe the syndrome is a manifestation of some structural or physiological disturbance of the sympathetic, that in some instances the symptom complex is perhaps analogous to some of the so-called smooth muscle spasms which are well known to be manifestations of an unstable sympathetic or vegetative nervous system — for example, paroxysmal tachycardia, pseudoappendicitis, pseudorenal colic, and certain types of

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spasm of muscles of the eyes controlling either accommodation or binocular vision.

Group A. Cases are patients with associated endocrine defect.

1. A middle-aged man with a hypothyroidism shown by a basal metabolism of —20, fatigability, slow pulse, dry skin, need for 10 to 12 hours' sleep in 24, constipation, and a gain of 60 pounds weight in four years.

During the time the patient had the hypothyroidism, he was subject to frequent brief attacks of pain, which was most severe below the ear, in the back of the upper part of the throat and in the right side of the hard palate. The pain frequently radiated to the back of the neck and the upper aspect of the right shoulder, and often it was accompanied by tearing from the right eye and salivation. When present, the pain would last for hours and as time went by the frequency of the pain increased so that it was present practically every day.

The hypothyroidism syndrome cleared up after thyroid feeding. The pain syndrome was unaltered by any treatment measures, although the physician in attendance reported 24 to 48 hours' relief after cocainizing of a sensitive spot in the lateral wall of the right pharynx close to the opening of the Eustachian tube. Successful injection of the stellate ganglion immediately stopped the pain, which gradually reappeared at the end of 24 hours.

2. A middle-aged woman with a history of migraine headaches, food allergy, oligomenorrhea, constipation, limited energy and on two occasions during an eight-year period a basal metabolism of less than —10.

She was subject to recurrent episodes of pain in the lower face on the left, over the carotid bulb and on the left side of the scalp, running down into the back of the neck and shoulder. With these attacks of pain she would have a watery discharge from the left nostril. The attacks of pain seemed to have no correlation with the menstrual cycle or her migraine. The attacks first appeared within a few months after an injury which produced symptoms and signs of a lesion in the lower cervical and upper thoracic segments of the cord.

With respect to the patient's constitution, there was a family history of thyroid disease in two individuals on the maternal side, diabetes on the paternal side, and alcoholism and suicide in three maternal antecedents.

3. A middle-aged woman with a very unstable emotional make-up and a tendency to hypochondriasis developed an abnormal gain of weight, fatigability, increased emotional instability and symptoms of digestive unrest. This syndrome continued for two or three years.

Then she began to have pain which she localized as in a left upper tooth, spreading to the lower jaw and radiating down the side of the neck. At times when the pain was severe, there would be a watery discharge from the left antrum, an unpleasant taste in the mouth and palpitation of the heart.

Basal metabolism was —17. Thyroid medication led to remarkable improvement in the entire clinical picture with the practical disappearance of the face and neck pains, which for the first time since their onset were absent for as long as two months.

4. A woman, age 42 years, had her right ovary removed because of a tumor when she was 18 years old, and the left ovary and uterus removed because of a tumor involving the left ovary at the age of 35 years. Then she began to have vertigo attacks, associated with nausea and palpitation of the heart. Her blood pressure dropped to a systolic level of less than 100.

At the age of 39 years she commenced to have headaches of two kinds. One variety occurred every four to five weeks; the pain was always in the left side of the head, commencing over the left eye, was of boring character, and usually occurred during the night and caused her to awaken from sleep. Nausea frequently accompanied the pain. Ergotamine tartrate was successful in cutting short the headache.

The other attacks of headache would commence in the right occipital region and radiate downward to the shoulder and forward to the right side of the nose, the right forehead and the right cheek. With these headaches, her entire face would become quite red, the right eye would seem dry and there was a lack of saliva. These attacks of pain would occur every week or oftener and at times would last for two days. Nothing would relieve the pain. Exposure to a cold wind would often precipitate an attack.

The patient suffered from pollen sensitization in August each year for about five years; strawberries would produce a rash on her neck, and oranges would cause nausea. The patient's hair turned gray by the time she was 35 years of age.

In the family history, the mother had suffered from rose fever and migrainous headaches until she was about 50 years of age. One brother had both rose fever and asthma in the later part of the summer. On the maternal side of the family, early graying of hair was common.

Sustained pressure over the right carotid bulb produced pain in the right suboccipital region and also over the right eye.

Group B. 1. A well balanced, healthy man, in his forties, developed cancer of the left side of the tongue, with metastases to the lymph nodes of the left side of the neck, particularly over the carotid bulb. Neck dissection was not feasible and the patient submitted to intensive irradiation, which resulted in fibrosis and contraction of the tissues in the neck. During the first few weeks after irradiation began, the patient developed severe pain, grinding and constant in character, which he localized as in the left temple, left cheek, under the left jaw and in the neck and shoulder. The pain spontaneously subsided, but reappeared several months later at a time when there was clinical evidence of recurrence of the metastases in the lymph nodes of the left side of the neck. There was no recurrence of the pain shortly after another course of irradiation, but in time, when the irradiation fibrosis became manifest, there was a recurrence of pain, which has continued during the past two years. This pain appears to be definitely reduced by ergot and gelsemium; it is not relieved by trichlorethylene, analgesics or narcotics.

2. An elderly woman developed carcinoma of the right tonsil. There were metastases to the lymph nodes of the neck with a large mass over the carotid bulb. As the mass increased in size there was local tenderness and pain, which commenced over the carotid bulb and radiated upward into the throat, hard palate and region of the maxillary antrum. This pain would be present intermittently for hours at a time and gradually became so constant that the patient could not rest. There was lacrimation from the right eye, and the right nostril became congested so that she could not breathe from it, when the pain was particularly severe.

Dissection of the neck resulted in a prompt disappearance of the pain.

I could extend this group of cases considerably because I have seen quite a number during the past 15 years at the Memorial Hospital.

Group C. 1. A man in his early fifties first developed pain in the region of the right maxillary antrum and the hard palate when he was about 30 years of age. The attacks of pain were paroxysmal at first and had the characteristics of true trigeminal neuralgia. As the years passed, the attacks of pain would last for weeks at a time, with sudden exacerbations

several times a day, the pain being constant the rest of the time. This patient would salivate and sweat on the affected side of his face. The pain usually extended to the side of the neck and shoulder, and there was tenderness of the carotid bulb.

During the past 10 years he has been subject to depressions, episodes of manic-depressive insanity. When in a depression, he does not seem to have pain.

2. A middle-aged woman suffered from attacks of migraine on the right side of the head and face. In 1928, she developed generalized convulsions, which were found to be due to paresis. In the course of treatment she developed a right hemiplegia. The attacks of migraine ceased.

In place of the migraine appeared episodes of pain, which she localized as in the right side of the roof of her mouth, radiating to the back of the neck and over the right shoulder and at times down into the right arm. She is also subject to epileptiform seizures, some of them petit mal in character, others definitely Jacksonian, with the movements starting in the right face and limited to the right half of the body, and followed by a period of confusion and anomic aphasia lasting an hour or more.

The trigeminal sensory root was severed without any effect upon the pain. Neither cocainization of the sphenopalatine ganglion nor a successful alcohol injection into the right stellate ganglion had any effect. Clinical judgment about this patient is complicated by a certain amount of organic mental deterioration and a constitutional emotional instability.

In atypical facial neuralgia the pain has certain somewhat characteristic tendencies. Superficial hyperesthesia or trigger zones are very much less definite than in true trigeminal neuralgia. The discomfort is described in varying terms — the pain is deep, boring, grinding or aching — and, although there may be transient exacerbations, the pain tends to be present for days or weeks at a time. Vasomotor and secretory phenomena are common. As a rule, the pain extends outside the area supplied by the trigeminal nerve.

In the cases described above, there were either systemic or local abnormalities indicative of endocrine or vegetative nervous system disorder. The frequency with which patients with this syndrome have tenderness of or complain of pain in the region of the carotid bulb has some diagnostic significance. The patients whose symptoms appeared to be related to neoplastic disease impress me as corroborative of the hypothesis that the pain syndrome represents a disorder of sensory fibres which are incorporated in vegetative or sympathetic fibres distributed along blood vessels supplying the head, face and neck.

The patients with definite endocrine defect would seem to be so constituted that some other form of vegetative dysfunction is related. The patient with manic-depressive epi-

sodes is of interest because of the apparent disappearance of pain during attacks of depression.

The patient with a history of migraine replaced by atypical facial neuralgia is perhaps difficult to evaluate because of the evidence of cerebral disease.

Most of the patients mentioned above have been thoroughly examined from the standpoint of their throats, ears and sinuses. A number of them have been treated for presumed sinus infection. None of these patients benefited from such treatment. Other patients with the same syndrome who have not been referred to in this paper give the same story.

Pottenger[1] refers to such pain as occurring in patients with upper lung disease.

Hyndman[2] concludes that the pain and hyperesthesia of postherpetic neuralgia are meditated by afferent sympathetic nerves, and that when the neuralgia involves the head or neck it may be eliminated by removal of the stellate and several upper thoracic sympathetic ganglia on the ipsilateral side.

Lewy and Grant[3] mentioned the differences in morphology and personality between patients with true trigeminal neuralgia and with atypical neuralgia.

Chavany[4] indicates that the pain is possibly due to an irritative or destructive lesion of the intra-axial sympathetic system, located high in the cervical region of the spinal cord.

CONCLUSIONS.

I have selected these cases to illustrate my belief that the syndrome known as atypical facial neuralgia is due to some structural or physiological defect in the sympathetic or vegetative nervous system. I have not tried to review the literature which supports my hypothesis.

The syndrome may be due to a variety of precipitating causes. In every patient one must search for and evaluate any clinical evidences of endocrine or vegetative nervous system defect.

Treatment falls into three categories:

1. The use of drugs which may have a palliative effect because of their action on the sympathetic nervous system.

2. Measures designed to improve some generalized or constitutional abnormality, including hormonal or endocrine therapy.

3. Surgery, directed either at the removal of some local precipitating cause or, in certain instances and perhaps as a last resort, in an attempt to interrupt the system of conduction of afferent pain fibres. This latter variety of surgery involves either the stellate and upper thoracic ganglia or a cordotomy in the midcervical region. I have no personal experience to report apropos of these more radical surgical measures, but other physicians have reported instances definitely indicating that these measures are effective.

Alcohol injections or surgery directed at the trigeminal nerve roots or ganglion are useless.

Treatment of teeth, sinuses or upper respiratory tract is futile unless there happens to be clear-cut evidence of adequate infection or other pathology.

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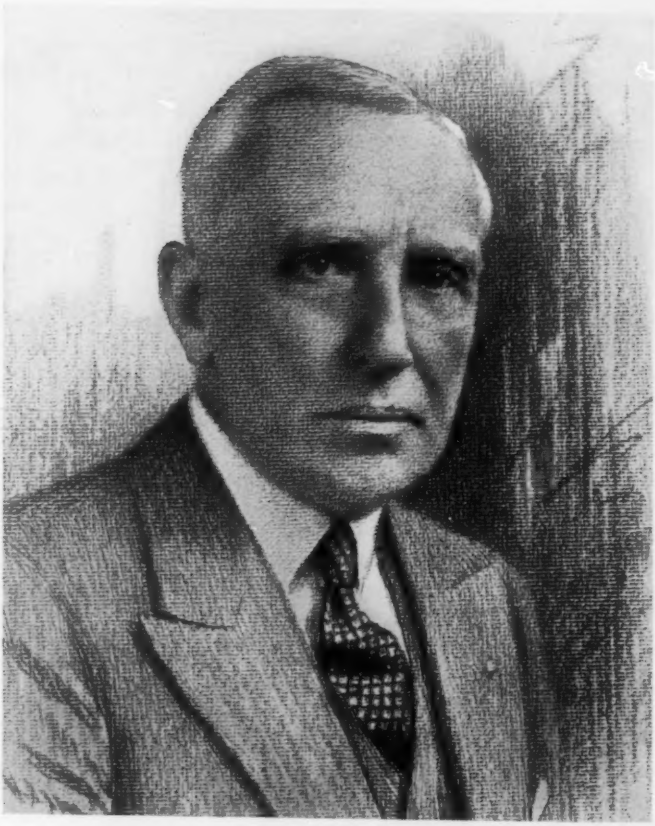

IN MEMORIAM

DR. MAX A. GOLDSTEIN,
1870-1941.

It is a sorrowful duty to report the passing of Dr. Max. A. Goldstein at his summer home in Frankfort, Mich., on July 27, 1941. Thus comes to an end the life and honorable career of a man who belongs to an era of fifty years in otolaryngology.

Dr. Max A. Goldstein was born in St. Louis, Mo., April 19, 1870. After graduation from the St. Louis High School and Missouri Medical College (now Washington University School of Medicine), in 1892, and a year's interneship at St. Louis City Hospital, he began the study of otology in Vienna under Dr. Adam Politzer, Dr. Victor Urbantschitsch and the other brilliant scientists who were active during that time of greatest progress in otology at the Austrian University.

During his active career he frequently returned to this fountain-head of science and maintained relations with these pioneers and their modern disciples. The two outstanding achievements of his career, THE LARYNGOSCOPE and Central Institute for the Deaf, had their inception in these early years of study. It was at this time that his great love for the literature of otolaryngology was born. For years, Dr. Goldstein devoted at least a short period of almost every day to perusing some old or new book on anatomy, medicine or surgery. Through this study he acquired an intimate knowledge of otological authors and their work.

Shortly after his return from study in the clinics of Berlin, Strassburg and London, and his establishment in the practice of otolaryngology, in 1896, he founded THE LARYNGOSCOPE, which he continued to edit and manage up to the time of his death. Dr. Goldstein was endowed with many requisites for editorship: A critical judgment, quick perception, a fine memory, a courageous and frank attitude toward contributors, an attractive personality, a resourceful and well

trained intellect; he was scholarly, vigorous and indefatigably industrious. All of these qualities combined with the good will and co-operation of his colleagues contributed to the growth and reputation of THE LARYNGOSCOPE. Its fifty-one volumes are an historical record of the progress of modern international otolaryngology. But few names that have enriched the literature of this specialty are missing from its pages, and it was Dr. Goldstein's pride that this journal was read in every civilized part of the world.

In 1895 he assumed the chair of otology at Beaumont Medical College, which later was absorbed by the St. Louis University Medical School and where he continued as professor of otology until 1912. For many years he was active in the clinics of this university and the Jewish Hospital of St. Louis. Here he often came in contact with deaf patients and, knowing the futility of medical treatment for many of them, he turned to the one avenue through which he could hope to benefit them: Education.

It was also in Europe that Dr. Goldstein's lifelong interest and devotion to the education of the deaf began. Returning from Vienna, where he had worked with Urbantschitsch on the new conception of education for the deaf, he found schools for the deaf in this country very inadequate. He felt the desperate need of a centre where little deaf children could begin their training under correct pedagogical methods, aided by the co-operation of the trained otologist. Such a partnership had not existed up to that time, and to meet this need he founded Central Institute for the Deaf, in 1914.

From an humble beginning of two teachers and four little pupils the Institute has grown into an internationally recognized centre where today 300 students from all parts of the United States and several foreign countries are enrolled.

Dr. Goldstein was an outspoken, courageous advocate of the Oral Method for training the deaf. When he began to publicize these views, that part of the orthodox profession still carrying on the teaching of signs to the deaf looked upon him as an interloper and a rebel. He took great delight in

reading the abuses heaped upon him, but he was convinced that results would be his best weapon. He lived to see his former denouncers accept his principles and become his admirers and friends.

One of the most important units at Central Institute for the Deaf, as envisaged by Dr. Goldstein, is its Training College for Teachers, for it was his ambition to see more and better trained teachers in schools for the deaf throughout the country. Through a grant from the Rockefeller Foundation the Teachers Training College of Central Institute for the Deaf inaugurated the first two-year professional curriculum for teachers of the deaf and speech defectives and became affiliated with Washington University.

These passionately loved activities of the Journal and Central Institute by no means robbed him of his interest in the practice of medicine, his major activity, and to this he was devoted for over forty years with enthusiasm. He made nearly 100 contributions to the literature of his specialty, outstanding among which were his two recently published books, "Problems of the Deaf," and "An Acoustic Method for Training the Deaf and Hard-of-Hearing Child."

Dr. Goldstein enjoyed his memberships in the various national otolaryngological societies; he attended their annual meetings with interest and eagerness and participated in many of their programs. During his forty-one years of membership in the American Laryngological, Rhinological and Otological Society he missed but five annual meetings, and read papers at twenty-one. Honors were not lacking in his life and he received wide recognition for his work. His otolaryngological colleagues bestowed upon him the Presidency of the American Academy of Ophthalmology and Otolaryngology, in 1902. He was President of the American Otological Society, Inc., in 1927, and of the American Laryngological, Rhinological and Otological Society, in 1931, receiving from the latter society the Gold Medal for Distinguished Service. The City of St. Louis likewise recognizing his service to the community, presented him, in 1933, with the Sec-

ond Annual Award for Distinguished Service to the city. The accompanying certificate designated him as an eminent otologist, scientist and writer. In 1937, Washington University conferred upon him the Honorary Degree of LL.D., for his pedagogic achievements.

As ardent as was his interest in his medical affiliations, just so was his devotion to educational organizations dedicated to work with the deaf and speech defectives. In 1917, he founded the Society of Progressive Oral Advocates, now the National Forum on Deafness and Speech Pathology. He was its first President and continued in this office for twenty-five years until the time of his death.

During the World War, Dr. Goldstein was a Major in the Medical Corps, serving as Chief of Head Surgery at Camp Dodge, Iowa.

He founded the St. Louis League for the Hard-of-Hearing and was a Director in the American Federation of Leagues for the Hard-of-Hearing, and also of the American Society to Promote the Teaching of Speech to the Deaf. He was President of the American Speech Correction Association in 1937-1939. He was keenly interested in the St. Louis Art League and served as its President in 1917-1919.

Dr. Goldstein could easily have filled his days with the usual experiences of the busy practitioner alone. Stirring within him was a creative mind and a spirit that knew no limitations of time and energy. He was endowed with a curiosity for knowledge which accounted for his versatility. Few moments of his life were wasted. He knew and loved the natural sciences; he knew and loved music; he knew and loved books, prints, drawings and paintings — but most of all he knew and loved the handicapped child. His slogan was "Help the Handicapped Child to Help Himself." To them he gave a selfless devotion and a fierce insistence on their rights to whatever assistance science could give them.

APPRECIATIONS.

Dr. Harris P. Mosher (Marblehead, Mass.):

Dr. Goldstein's career was one of the brightest examples of high achievement, in the specialty of otolaryngology, due to his great talent, unflagging perseverance and singleness of purpose. His sympathy and understanding early went out to those whom fate had deprived of half of their birthright; to those born deaf. To most of us these cases were hopeless, and we passed by on the other side. It was not so with Dr. Goldstein. In the treatment of these cases all of us marveled at his patience and envied his results.

There was a telepathy between him and his young patients so that they sensed their loss and co-operated willingly in all measures instituted for their amelioration. This was very evident as you saw him surrounded by his young pupils and to me was most striking.

The humanitarian side of his work did not obscure the scientific side; this was of the highest order, often pioneering in character. His work on the practical and applied side was equally outstanding, two conspicuous examples being the establishment, in 1914, and maintenance of Central Institute for the Deaf and THE LARYNGOSCOPE, *an international journal on diseases of the ear, nose and throat, which he founded in 1896.*

His personality was keen and incisive. He wrote clearly and spoke well. This was to be expected because he taught others to speak. It always amused me a little and excited my envy as well to see him discard with contempt the microphone on which all of the rest of us were so dependent. It was no boast on his part, because he always made himself easily understood.

Dr. Goldstein was broader than his specialty, as shown by his interest in old medical books. Of these he had a goodly collection, and it was a treat to have him show them and talk about them.

Fortunately, he trained many teachers at Central Institute for the Deaf who will carry on his work and keep his name alive.

I know no other physician who had and deserved fuller and more lasting gratitude from his patients.

St. Louis League for the Hard-of-Hearing:

Like thousands of others, we shall mourn his passing but know that the good he did while on earth will live after him and that his influence and inspiration will continue.

Dr. Walter Stevenson (Quincy, Ill.) :

It truly may be said that Max was a great man, and he left this world better off for having lived.

Dr. Ernest M. Seydell, President of the American Otological Society, Inc. (Wichita, Kan.) :

Otology has lost a very true friend and servant whose splendid contributions will not be forgotten. Though he will be missed by all otologists, the members of the American Otological Society will feel his loss especially.

Dr. Thomas J. Harris (New York) :

Max's friendship and mine goes back to our early medical life. My admiration and regard for him constantly have grown. I have looked with amazement at all that he has accomplished in his busy life. THE LARYNGOSCOPE itself is a *monument to him — much more, Central Institute for the Deaf, which stands by itself.*

Mr. D. W. Morris, Secretary, American Speech Correction Association (Terre Haute) :

I am personally and professionally grateful to have known Dr. Goldstein; his scientific and educational contributions have lent depth and dignity to our profession. Those of us in the younger generation will find our tasks easier because of men like Dr. Goldstein and will reap the fruitful reward of widening public recognition of the work of his lifetime.

Dr. Gordon Berry (Worcester, Mass.):

The otological world and the deaf children will miss him sorely, as will his many, many friends.

Dr. E. Lawrence Keyes (St. Louis):

Dr. Goldstein was a grand person indeed and one who will never be replaced. It was always a pleasure to talk to him and to marvel at his learning and constant enthusiasm.

Dr. Stacy Guild (Baltimore):

The death of Dr. Goldstein leaves a gap in the ranks which can never be completely filled. Specialization has advanced so far during the span of his life that no one nowadays gets the really broad training it was his privilege to have. Added to his natural talents, it made him the wonderful man he was, actively interested in all aspects of the problems of deaf people. To him they were not merely more patients, but each was an individual to be helped.

Mr. R. Wilson Brown, Superintendent, Missouri School for the Blind (St. Louis):

The passing of Dr. Goldstein means a tremendous loss to the entire field of the education of the handicapped. His great work of international character will stand forever as a memorial and inspiration.

Wm. B. Ittner, Inc. (St. Louis):

The far-reaching significance of his contribution to human happiness, as well as to scientific knowledge will, of course, be recognized more and more as time goes on. Surely, he leaves to posterity not only an original and distinctive medical achievement but, what is more important, a record as a benefactor to mankind, especially to handicapped youth. How truly it can be said of him that "he left the world better than he found it."

Dr. C. Stewart Nash, Secretary, American Laryngological, Rhinological and Otological Society (Rochester, N. Y.):

Dr. Goldstein was one of our most loyal and esteemed members. The society will miss his active support but is grateful that it has had so distinguished a member.

Dr. J. A. Bronfenbrenner, Washington University School of Medicine (St. Louis):

No life can have been a greater creative force for the welfare of his community and humanity everywhere.

Mrs. Bess McClure (Springhill, Ala.):

We mothers can never be grateful enough to him for what he has done for the deaf.

Dr. Maurice Levy (Denver):

Not often does it fall to the lot of one human being to be responsible for as much happiness and constructive good as Dr. Goldstein was able to do.

Dr. Wm. H. Haskin (New York):

What a glorious career he had and what inestimable blessings he conferred upon so many afflicted beings!

Mrs. S. M. Benderoff (New York):

He will always live in the hearts of parents and children whom he befriended.

Dr. Herbert S. Birkett (Montreal):

To the profession and to the deaf who benefited from his great skill his loss is irreparable, for in the education of the deaf he was recognized as a world authority. Not only was he outstanding for his knowledge and his ability, but he exemplified what is the noblest attribute of a physician, that in all he did he was prompted by the highest motives, and did not spare himself in the service of suffering humanity. There are few like him in the profession today.

Dr. George M. Coates (Philadelphia):

The whole profession will mourn for him, but his monument will be Central Institute, his writings and the gratitude of his patients.

Miss Betty Wright, Executive Direction, American Society for the Hard-of-Hearing (Washington, D. C.):

His interest in those with impaired hearing was deep and sincere. We feel that the deaf and the hard-of-hearing have lost a real friend.

Dr. Emil Amberg (Detroit):

He was an integral part of the otology of our time.

Dr. Clarence D. O'Connor, Superintendent, Lexington School for the Deaf (New York):

He was one of the great leaders and pioneers in our profession, and his death will be a personal and a professional loss to all connected with the work he loved so much.

Dr. M. D. Lederman (New York):

The profession mourns the passing of a distinguished scientific student whose modest personality was one of his fine qualities. We have lost an affectionate friend of over fifty years' association.

Dr. James A. Babbitt, President, American Laryngological, Rhinological and Otological Society (Philadelphia):

It seems a tragedy to lose so useful a man.

Dr. Ralph A. Fenton (Portland, Ore.):

It has been a great pleasure to know and honor him. His work, especially for the deafened, will live on and his personal charm and brilliance will adorn his memory.

NEW YORK ACADEMY OF MEDICINE.

SECTION ON OTOLARYNGOLOGY.

Regular Meeting, Dec. 18, 1940.

(Continued from June issue.)

Sulfanilamide in Otitis Media in Children. Further Report on a Controlled Series. Dr. Edwin B. Bilchick and Dr. George Hunter O'Kane.

(To be published in a subsequent issue of THE LARYNGOSCOPE.*)*

Tonsillectomy. Conservation of Tissues, Fascia and Mucosa. Dr. Robert H. Fowler.

(To be published in a subsequent issue of THE LARYNGOSCOPE.*)*

DISCUSSION.

Dr. ——— asked about the relationship of the flap to hemorrhage.

DR. FOWLER: Nothing would have given me greater pleasure than to say to you, "Gentlemen, we have discovered that at one step we can relieve all the difficulties of the tonsil operation." However, that is not what I have said, for it is not the truth.

You are presented with a plan for a plastic flap which after 2,000 operations appears to have advantages as such. But it is not a cure-all. To mix it up with our treatment of hemorrhage would be a mistake and might bring it into disfavor if it were offered as solving the problems of postoperative bleeding. Quite the contrary is true. Tying the flap to the main vein may at times lead to postoperative bleeding of that less severe type that is apt to occur four or five days after operation. Apparently this is because the traction on the knot is apt to dislocate it from the vessel.

Therefore, I have been careful to state that on the basis of experience, as well as on the basis of theory, we cannot expect as good results as regards postoperative bleeding if we leave the same tie which anchors the flap, to control it, as though we treat the two matters separately.

Indeed, gentlemen, it is my conviction that in hemorrhage we have the one great difficulty remaining in tonsil surgery. Control of bleeding is complicated by the fact that there are several vessels to be considered.

Dr. Babcock, our Chairman, will bear me out in this, for he made a research on the arterial supply of the tonsil.

If we expect a plastic flap to do a magic and stop bleeding, either under or at the edge of the flap, we will be disappointed. Tie off the vessels, and use a separate knot for the main vein, or run the risk that you may have to see your patient again.

However, in this series of 2,000 cases there were no fatalities, no hemorrhages that required transfusion or ties on the carotid. There were only the lighter types of bleeding, but these were carefully recorded, and analysis of 800 showed postoperative bleeding in 5 per cent on children and 7 per cent on grownups when the same catgut tie was used for vessel and flap.

STATISTICS RE FLAP OPERATION, JAN 1, 1934, TO DEC., 1940.

Women — General	266		
Women — Local	72		
		338	1934 — 141
			1935 — 114
Men — General	168		1936 — 150
Men — Local	39		1937 — 146
		207	1938 — 100
			1939 — 105
Girls — General	134		1940 — 52
Girls — Local	7		808
		141	
Boys — General	122		
Boys — Local	.....		
		122	
Operations: Total		808	

Total — Adults	545	Operated	Adults	.071	Bleeding
Total — Children	263		Children	.051	

BLEEDING.

W. G.	W. L.	M. G.	M. L.	Child G.	Child L.	Adults	Child	
3931	.....	3870	3947	.....		3—0		1934
4313	.....	4331	.....	4362		4—1		1935
4315	.....	.....	.....	.....				
4325	.....	.....	.....	.....				
4619	.....	4488	4722	.....		8—0		1936
4727	.....	4652	.....	.....				
4754	.....	4742	.....	.....				
.....	4919	5133	5095	4853		3—2		1937
.....	.....	.....	.....	4929				
5272	.....	5338	5208	5147		3—8		1938
.....	.....	.....	.....	5212				
.....	.....	.....	.....	5231				
.....	.....	.....	.....	5313				
.....	.....	.....	.....	5315	NONE			
.....	.....	.....	.....	5320				
.....	.....	.....	.....	5324½				
.....	.....	.....	.....	5334½				
5494	.....	5470	.....	5376		2—5		1939
.....	.....	.....	.....	5439				
.....	.....	.....	.....	5480				
.....	.....	.....	.....	5521				
.....	.....	.....	.....	5555				
5637	.....	5650	.....	5652		5-3		1940
5671½	.....	.....	.....	5694				
5692	.....	.....	.....	5748				
5719	.....	.....	.....	.....				
Totals— 14	1	9	4	19		28	—	19

Total Bleeding of Group — 808 Cases — 5.7% — Adults 7.1% — Children 5.1%

DISCUSSION.

QUESTION: How about postoperative hemorrhage?

DR. ROBERT H. FOWLER: Nothing would give me greater pleasure than to be able to say to you that in all respects this was a perfect procedure; that, however, is not the fact. It is better in our research for truth to be accurate and scientific.

What I present is a plan for a plastic flap in tonsil surgery designed to improve repair. When carried out as described in this paper it does exactly this: it diminishes the discomfort by half; it shortens the time of covering in the fossa; it gives the patient the chance to eat breakfast the next morning. But it is not a cure-all. To mix this step up with our treatment of hemorrhage would be a mistake and would bring it into disfavor if it were offered as solving the problems of postoperative bleeding. Quite the contrary is true. There may be times when tying the flap edge to a large vessel puts tension on the tie.

In my series of 2,000 cases, the number of postoperative hemorrhages is not markedly different from the average in my own operations. The figures here given show about 6 per cent of the cases have some slight bleeding after operation, and this is about what might be expected. In all these cases, hemorrhage was easily controlled, there were no serious difficulties, no transfusions were required, nor tying of the carotid. But when we are required to give the patient further attention on account of bleeding in every eighteenth case, it is evident that the final solution of minor hemorrhages has not yet been reached.

The flap is a success when used for report, but will be found disappointing if we attempt to combine the added function of controlling hemorrhage to that of repair of the wound.

DIRECTORY OF NATIONAL OTOLARYNGOLOGIC SOCIETIES.

American Otological Society.

President: Dr. E. M. Seydell, 107 W. Douglas Avenue, Wichita, Kan.
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Executive Secretary: Dr. William P. Wherry, 1500 Medical Arts Building, Omaha.
Place: Chicago. Time: Oct. 19-24, 1941.

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